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TREASURY CONTROL AND SCIENTIFIC RESEARCH

IT has been apparent for some years, both from continued questions in the House of Commons and from the reports of the Select Committee on Estimates and the Committee of Public Accounts, that the House of Commons is increasingly concerned about the expenditure of the Department of Scientific and Industrial Research and of the University Grants Committee. The criticism advanced has not been unfriendly, for there has been no indication that Parliament wishes to restrict expenditure on scientific and industrial research; on the contrary, it is generally recognized that this should be expanded but that more care should be taken to ensure that full use is made of the results of such research. The Treasury has stoutly defended the autonomy of the universities and refused to agree to any proposals that appear likely to endanger their independence and freedom to determine the nature and balance of their work, and the reorganization of the Department of Scientific and Industrial Research, following the report of the Jephcott Committee, may be regarded as a sequel to some Parliamentary criticism of the Department.

Although the Treasury has made some concessions in regard to the expenditure of the Vote for the Department which give more freedom for the planning of research over a period of years, it would not appear that the problem of the control of expenditure on research, even in general terms, is fully understood by Parliament. A recent report from the Select Committee on Estimates (see *Nature*, October 25, p. 1111, and November 1, p. 1181), which was devoted to the work of the establishments of the Department, showed a concern with expenditure, particularly with the recovery of expenditure from those who had benefited by it, which could well prejudice the planning and support of the Department's programmes of research and even warp their direction. Furthermore, although the third report from the Committee of Public Accounts for the session 1957–58 fully exonerated the consulting engineers for the Jodrell Bank radio-telescope from failure to consult with the University professor in charge of the project, it is disturbing that the Committee should have advanced its criticism last session without inviting evidence from the University of Manchester or from the consulting engineer in charge of the building project. To say the least, the Committee of Public Accounts has shown little awareness of the dangers of waste and delay which may arise in such undertakings from the too rigorous application of financial accounting through estimates.

The latest report, while admitting that the previous report was ill-informed, gives no clue as to why and where the Committee regards the financial control exercised over the scheme as unsatisfactory. It welcomes the assurance that the remaining money required for the construction of the telescope will not be met, directly or indirectly, from public funds, but will be found from other sources by the University (see p. 1484 of this issue). There is no evidence that public money has not been properly and openly spent on the project, and equally no recognition of the difficulty of providing in advance firm estimates of cost for the construction of such novel equipment.

This is the most disturbing aspect of the report from the Committee of Public Accounts. It is vital that this affair should not deter other universities from entering on big building projects, or discourage the Department of Scientific and Industrial Research from its statutory duty of fostering fundamental research. Scientific research has come increasingly to depend on expensive equipment, the construction of which is often as much beyond the resources of individuals as it is beyond their capacity, without co-operation from others, to keep it fully and economically employed. As already noted, there appears to be a danger that the Estimates Committee may also divert the Department from the most fruitful discharge of its responsibilities.

Nor can we regard the danger as likely to be eliminated entirely if greater efforts are made in the matter of publication either through annual reports or in other ways. Attention to some comments of the Estimates Committee on this point should go some way to avoid unhelpful and misinformed criticism in Parliament, and might well provide the most effective solution to the real problem of public accountability. The reports of these two Parliamentary Committees demonstrate the urgency of this issue; but they equally show how imperfect and inadequate either the Committee of Public Accounts or the Select Committee on Estimates is as an instrument for the control of expenditure on such matters as research and development, though, as Basil Chubb showed clearly in his study of these Committees, that is not their function.

The whole question of Treasury control was examined by Prof. S. H. Beer in a thoughtful study published two years ago. He was not concerned with the practical aspect of its appropriateness to the needs of to-day, but, for the reasons just given, the more limited examination of Treasury control of expenditure in the sixth report from the Select Committee on Estimates for the session 1957–58* is of profound interest to the scientist and technologist at the present moment. Primarily the report is concerned with the methods of Treasury control employed and their effectiveness, rather than with actual expenditure, with the view of discovering whether they are such as to ensure economies in the Estimates, and attention is concentrated on control over supply expenditure, in contrast to establishment expenditure, which the Committee considers should be further examined. The latter relates to all expenditure on personnel remunerated from public funds, and since supply expenditure covers

* Sixth Report from the Select Committee on Estimates together with the Proceedings of the Committee, Session 1957–58: Treasury Control and Expenditure. Pp. 42. (London: H.M. Stationery Office, 1958.) 2s. net.

all other types of expenditure, it includes that on new projects such as the Jodrell Bank radio-telescope. This is nowhere discussed in the report; but for the scientist and technologist, one of the most important sections is that which discusses the way in which the Treasury exercises control by prior sanction of new projects and how it functions in practice.

First, it is important not only to scrutinize new policies but also to review carefully current policies. The Committee recognizes that it is uneconomical to cut a good new policy while a less-worthy policy is allowed to carry on without modification; but it found little to suggest that established policies are sufficiently reviewed and is disturbed at the absence of evidence of a constructive approach which would ensure that the reasons for continuing a policy or programme were independently and systematically sought. This is particularly important in regard to scientific and technological research, and it is in line with criticism from the Committee of Public Accounts and elsewhere that the Estimates Committee recommends that the Treasury should ensure that established policies in the civil field are more systematically reviewed.

It might well be asked whether this should be the function of the Advisory Council for Scientific Policy, or, in matters of defence research, of the Defence Research Policy Committee; and that could also apply to the second matter on which the Committee expresses concern. While it appreciates the difficulty of accurately estimating the cost of a novel policy or of research or development on a totally new type of weapon, and welcomes the appointment of a committee to consider and make recommendations about methods of managing and controlling research or development projects as likely to lead to more accurate estimating in this field, it rightly insists that sound decisions can only be taken on the basis of accurate estimates. The Committee suggests that supplementary estimates, due to the practice of under-estimating, can largely destroy effective budgetary control both of the national economy and of Government expenditure.

The third matter that caused the Estimates Committee some concern is the natural tendency, within the present annual system of Estimates and Accounts, to concentrate too much attention on the policy and expenditure proposals for the coming financial year, with too little regard to the commitments and consequences for future years. Such obsession can stultify forward planning, and it is the more serious in the context of the tendency to under-estimate the costs of policies and major projects. While the Ministry of Defence and the Treasury have recently introduced a practice of preparing—each summer—forecasts for three years ahead, on the basis of current policy, of the total and major features of defence expenditure, the Committee is disappointed that there seems to be little parallel effort on the civil side. Forecasts alone are not enough, though the defence forecast for the next year, when approved by the Government, becomes the defence budget on which that year's estimates are based; and the Committee urges that such a dynamic approach to expenditure should also be made in the civil sector.

In discussing next the way in which Treasury control operates over programmes of expenditure and annual estimates, the Estimates Committee appears to recognize fully that it is necessary for certain purposes, such as university grants or the Department of Scientific and Industrial Research, to allocate expenditure for several years ahead, and it endorses the increased departmental responsibility which is involved in such a practice. It suggests, however, that in some fields programmes might be made more specifically schedules of work to be done, and that while the department is probably the best judge of priorities, the need for capital works should be justified to the Treasury. Without making specific recommendations, it suggests that such specific programming might offer advantages in major research and development work where needs can be anticipated.

A large part of the Committee's inquiry was devoted to hearing evidence about the merits of the control which the Treasury exercises by prior sanction of new projects, its effectiveness in achieving economies and the degree to which financial authority could be and has been delegated to spending departments. In view of the high proportion of Government expenditure which is now required for highly technical projects, the Estimates Committee rightly attaches great importance to these questions. Under the traditional system, such projects are not vetted by any technical officer except those responsible for initiating them, and it is obvious that the Estimates Committee has grave doubts as to the effectiveness of prior sanction control by the Treasury.

The Treasury does not employ professional or technical experts, and the value of such control depends accordingly largely on the skill with which the Treasury officer can criticize a proposal submitted by departmental officers who may have spent their entire working lives dealing with that subject, or a highly technical project submitted by a technical expert. Such lay critics are not necessarily ignorant—and the educational system could reduce the risk of them being so—and it may well be beneficial to require the expert to justify his claim for money to a man of general common sense and broad understanding. Nevertheless, the Treasury critic may well feel inhibited in some circumstances, and be limited to judging whether a need is proved. The Committee found little indication that Treasury scrutiny made departments less meticulous than they should be in their own scrutiny, but it points out that this reliance on laymen encourages, and certainly makes possible, attempts to blind the Treasury with science in relation to some types of project. It does not think that the method will work unless technical men play their part in discussions with the Treasury, and recommends accordingly that more attention should be paid to the advantages of associating technical officers with financial decisions. It is rightly observed that an awareness by technical officers of the financial implications of their proposals is an essential feature

of a system which places a large measure of economic responsibility within spending departments.

The Estimates Committee does not, however, suggest the abandonment of control by prior sanction entirely, though it recommends some relaxation of its exercise, particularly when the expenditure is part of a specific policy decision approved by the Cabinet or Treasury or is a matter of detailed administration, or again when the raising of the financial ceiling will not remove a major field of departmental expenditure from Treasury control. It suggests that control could also be relaxed where greater use is made of the technique of control of expenditure by programmes as already indicated; but it also points out that there are highly important and far from standard projects where inaccurate estimates are frequently made, and the Treasury has shown that its scrutiny can lead to economies, of which the Treasury is not seeing enough.

While on balance the present system appears to work reasonably well, and it is probable that much more expenditure is wasted through political decision or indecision than from the weaknesses which are noted by the Estimates Committee, on the evidence already discussed the Committee appears to be fully justified in its recommendation of a full inquiry into the theory and practice of Treasury control of expenditure. What is debatable is whether the small independent committee, with access to Cabinet papers, which it recommends will suffice, or whether the inquiry should not rather be entrusted to a Royal Commission. To the question whether the existing practice is as effective as modern conditions demand, it gives no definite answer, although it makes a number of suggestions for improving the system.

Some of these have already been noted, and others are made in considering the Treasury's interest in continuing expenditure, where the Committee again points out the danger that Supplementary Estimates or increases may divert attention from areas of expenditure which should be decreasing because of reduced demand, or because the costs of running an established service are lower than those of initiating it. While it recognizes that Supplementary Estimates are no longer regarded as discreditable, no positive proposals are made for dealing with this difficulty, which so far as the technical projects are concerned might well involve bringing technical experts into the Treasury, much as has been done in the Organization and Methods Division, and possibly developing a Division competent to say which new increases in departmental expenditure should be offset by new economies and which covered by Supplementary Estimates. Such a device might well have avoided the difficulty over the radio-telescope at Jodrell Bank, and need not involve serious delays.

For the rest, the Estimates Committee emphasizes the undesirability of leaving all initiative for economy to the departments, and the value of continuing Treasury interest. It is not satisfied, for example, that the Treasury takes sufficient interest in how grants-in-aid are spent or the services administered—apparently the attack on the University Grants Committee is only suspended. On research and development for defence purposes, it recognizes both the difficulty of control and the effect on the demand for skilled man-power and the critical resources of industry. The estimated expenditure for research and development by the Ministry of Supply alone this year exceeds £211 million, and it is vital to get the balance of effort right. With the pressure of demand on limited resources, it is not enough to examine new projects. Research and development programmes also require regular and careful combing to remove projects which have proved abortive and also those that have already produced most of the results that could be expected of them.

The crucial question is how such scrutiny and pruning are to be effected. Inevitably the Treasury relies chiefly on the scientific advisers to the departments, and the Chief Scientist of the Ministry of Supply said that the biggest and most effective action in reviewing research came from the pressure on scientific branches and establishments to do more and more tasks with limited funds and man-power. In consequence, they were always reviewing programmes and cutting out anything that did not seem to be sufficiently profitable. In other words, the pruning of projects is best undertaken by those responsible for the projects; but their views may be too narrow, and accordingly reviews by the Defence Research Policy Committee or, in the civil field, the Advisory Council for Scientific Policy, are also desirable. The investigation now being made by Sir Claud Gibb's Committee may result in the Treasury becoming better equipped to judge the value of defence research and development work that has already been authorized; but the Estimates Committee's report does not suggest that however effective Treasury control may become it will eliminate the need for such co-ordinating bodies.

The Estimates Committee's report indeed leaves grave doubts as to whether, in fact, either the Defence Research Policy Committee or the Advisory Council for Scientific Policy is functioning effectively. It is on bodies of this character that we must rely for the wide and expert views which can ensure that the scientific and technical effort of Britain is in balance, and that the demands on man-power and resources as well as on finance made by one sector are not out of proportion or impeding vital effort elsewhere. There, if anywhere, should be awareness that no country to-day can undertake every scientific or technological project at once. How this co-ordination is to be effected is a problem of the first magnitude to which urgent attention should be given. Some of the proposals of the Estimates Committee may help, but a fundamental condition of effective control will remain a real public understanding in Parliament, in the Government, in the Civil Service and among the general public of the nature and needs of scientific and technological work. To that a sound and effective publication policy could contribute, but the decisive factor in the end will be the development of an educational system adequate to the needs of a changing technological age.

ENCYCLOPÆDIA STATISTICA

The Advanced Theory of Statistics

By Prof. Maurice G. Kendall and Alan Stuart. Vol. 1: Distribution Theory. (Three-volume edition.) Pp. xii+433. (London: Charles Griffin and Co., Ltd., 1958.) 84*s*.

FIFTEEN years ago, Prof. M. G. Kendall published the first of two volumes that rapidly established themselves as indispensable to statisticians. Even critics who disagreed with some of the controversial views expressed and found flaws in points of detail not only were bound to admire Kendall's versatility in his comprehensive coverage of mathematical statistics but also came to accept the books as standard works of reference. These fifteen years have seen consolidation in some fields, reduction of emphasis in others, new lines of theory, and above all new understanding of the inter-relations between parts of the subject. In the preparation of a completely revised and re-set edition, Prof. Kendall has had Mr. A. Stuart as collaborator. This edition is to appear in three volumes; the magnitude of the task can be appreciated from the fact that Vol. 2, "Statistical Inference and Statistical Relationship", is planned for publication in 1960, and for Vol. 3, "Statistical Planning and Analysis, and Time Series", no date has yet been given.

Evaluation of one volume alone is unsatisfactory, because the balance of the whole work cannot be judged. The first twelve chapters are essentially the same as the first eleven chapters in the previous Vol. 1, but have many sections improved in rigour or brought up to date. Frequency-generating functions, a surprising omission previously, are now employed to good advantage. Changes of emphasis on systems of distributions are typified by the virtual omission of the Charlier type-*B* series and the inclusion instead of a good summary of the lognormal distribution and Johnson's transformations. The presentation of the calculus of probabilities is now much clearer; statement of the weak and strong laws of large numbers is one aspect of its improved coherence, yet the authors' practical contention that "In statistics it is a mark of immaturity to argue overmuch about the fundamentals of probability theory" is well maintained. In many places, as in the discussion of distributions of ratios of statistics, groups of related topics are better integrated than before. The long account of *k*-statistics and symmetric functions, inevitably somewhat tedious reading to those who lack special interest in it, is none the less an excellent account of a subject to which Kendall has himself made outstanding contributions; formulae appropriate to finite populations are now included, and the new Chapter 13 develops generalizations to bivariate distributions.

Since publication of the first edition, one major growth of statistical theory has been in connexion with order statistics and non-parametric analysis. The ultimate importance of this work to statistical thought cannot yet be assessed, but an excellent survey of its main themes rightly appears as a new chapter. A good account of multivariate normal theory from a modern point of view forms Chapter 15, and a final chapter summarizes the derivation and properties of the main distributions associated with the normal.

Although courses of instruction in statistical theory can well be based upon this book, as an aid to which more than 300 exercises (mostly fairly difficult) are included, a majority of statisticians will probably value it and its successors chiefly as an encyclopædia. Not only are the main lines of development of theory clearly presented, but also the authors embroider their account with mention of many topics of lesser importance; to have these recognized and made more accessible than in past volumes of journals adds greatly to the interest and value of "Kendall and Stuart" as a work of reference. Indeed, my own regret is that space has not been found for a still greater range of minor themes: references to books and papers listed in previous editions but now excluded as falling outside the stream of current statistical thought could still have been justified for encyclopædic purposes. One fault, perhaps inevitable in an encyclopædia, is the emphasis on facts and the comparative neglect of discussion of the circumstances in which these facts are useful. The sections on χ^2, for example, are still somewhat perfunctory, and no reader would guess from them that the uses of this statistic in the analysis of observational records are so diverse.

Prof. Kendall has placed all statisticians in his debt for the breadth of his publications during the past fifteen years; the next two volumes in this series will be awaited with interest and with the hope that all will continue to be so conscientiously revised as statistical theory continues to grow.

D. J. Finney

THE SCATTERING OF LIGHT BY SMALL PARTICLES

Light Scattering by Small Particles

By H. C. van de Hulst. (Structure of Matter Series.) Pp. xiii+470. (New York: John Wiley and Sons, Inc.; London: Chapman and Hall, Ltd., 1957.) 96*s*. net.

THE problem of the scattering of electromagnetic radiation by a homogeneous sphere, to which partial solutions in particular cases were provided by Rayleigh and others towards the end of last century, was finally solved by Mie in 1908. The application of the formal Mie solution presents great difficulties. The series in which it is expressed may converge slowly, and the investigator who seeks to apply the formula to a particular problem is therefore fortunate if he finds ready-made tables or curves for the scatter functions relevant to the refractive index and ranges of the ratio of radius to wave-length with which he is concerned.

It was in 1945, while Dr. H. C. van de Hulst was investigating the effects of interstellar dust, that he became aware of these difficulties and was led first to undertake a thorough review of the literature and then to make important contributions himself, both to the theory and to filling the gaps by new computations. In this valuable book, he has assembled in an admirably clear and logical manner the results of his work of reviewing, and of his own further independent studies of, this very complex subject.

Van de Hulst confines himself to the theory of 'independent scattering', that is, to the scattering by particles sufficiently distant from each other that "for all practical purposes, the intensity scattered by the various particles must be added without regard to phase". It appears that separation by a distance as small as three times the radius yields independent

scattering; actually, in a dense fog, the mutual separation is of the order of twenty times the radius of the droplets. He imposes the further limitation that 'single scattering' alone is considered, the criterion for this (that is, for the absence of 'multiple scattering') being that doubling the concentration of particles in a sample doubles the scattered intensity.

The first of the three parts into which the book is divided is concerned with the development of general theorems for scattering by particles of arbitrary size, shape and composition.

The second part provides the theory necessary for the calculation of the scattering for a wide variety of special particles large and small compared with the wave-length, absorbing and non-absorbing, and of various shapes. This is by far the largest and most important part of the work and is the section that is certain to be widely consulted by applied scientists seeking aid with numerical calculations. Nearly every chapter contains new formulæ and numerical results, and a valuable bibliography of numerical computations by the Mie theory is provided. There is an excellent chapter on the optics of a raindrop which includes a penetratingly critical review of theories of the rainbow and a full account of the theory of the glory, extended in a later chapter by a brief examination of the effect of the existence of surface waves.

The final part of the book consists of four short chapters on the practical application of the theory to the explanation of scattering phenomena in the domains of chemistry, meteorology and astronomy, and on the use of scattering and extinction measurements to derive estimates with varying accuracy of refractive index, size and distribution of sizes, shape and orientation, and chemical composition of the particles.

A valuable feature of this outstanding book, which should be the standard work for many years, is the comprehensive list of carefully annotated references at the end of each chapter. JAMES PATON

COMPLEXOMETRIC ANALYSIS

The Analytical Uses of Ethylenediamine Tetraacetic Acid

By Prof. Frank J. Welcher. Pp. xvii+366. (Princeton, N.J.: D. Van Nostrand Company, Inc.; London: D. Van Nostrand Company, Ltd., 1958.) 64*s*.

AN important development in chemical analysis during recent years has been the application of aminopolycarboxylic acids, especially ethylenediamine tetraacetic acid, as complexing agents. Many publications concerning the analytical uses of this acid have appeared, and Prof. Welcher's book provides a summary of information gleaned from the 963 bibliographical references listed at the end.

The author states that he has endeavoured to collect information from all papers describing the use of ethylenediamine tetraacetic acid in inorganic analysis, but that critical evaluation of each method has not been attempted and that the book is not intended as a manual of recommended methods, though details of many procedures are given with reports on interference, optimum conditions, and claims as to accuracy.

The book opens with a discussion of general principles, including complex-formation constants, titration methods, colorimetric determinations, and the effect of *p*H on complex-formation. Succeeding chapters provide much information concerning end point detection, metal indicators, the use of masking agents, the determination of more than thirty metals, indirect methods for anions, and applications to polarography, amperometry, and qualitative analysis. Two chapters are devoted to the determination of calcium and magnesium in water and in a great variety of materials ranging from alloys, cements, and rocks to biological fluids and foods.

The subject-matter is mainly concerned with volumetric applications of ethylenediamine tetraacetic acid, but an interesting final chapter concerns the uses of the reagent to complex interfering ions, and thus facilitate more orthodox analytical work such as the colorimetric determination of bismuth, cobalt, and copper with diethyldithiocarbamate, the determination of mercury with dithizone, the spectrophotometric determination of beryllium in the presence of aluminium, the mannitol–boric acid titration in the presence of iron and other metals, the separation of the rare earths, and the gravimetric determination of uranium in the presence of other metals.

This book will be a very useful guide for the analytical chemist, though, as the treatment is mainly non-critical, many of the methods dealt with will call for some preliminary trials before being accepted for any specific purpose. However, this is in no way a criticism of Prof. Welcher's comprehensive compendium, which will be of the utmost assistance to those interested in the analytical chemistry of ethylenediamine tetraacetic acid. C. O. HARVEY

NOISE

Principles of Noise

By Dr. J. J. Freeman. Pp. x+299. (New York: John Wiley and Sons, Inc.; London: Chapman and Hall, Ltd., 1958.) 74*s*. net.

DURING the past few years considerable attention has been focused on the problem of detecting ever smaller signals; this requirement has been forced upon us from a number of quarters, prominent among which are radio, astronomy, and electromedicine.

The detection of these small signals is accompanied by the desire for a theory applicable to the random fluctuations with which the signal may be associated. Although investigations into electrical noise date back to Johnson's classical paper in 1928, until recently there have been very few books written in an attempt to integrate knowledge throughout the whole field of noise, and even fewer which have approached it in a tutorial manner designed for a reader with little previous knowledge of the subject. This is the task which the author has set himself.

The preamble to his book consists of two chapters dealing with the fundamental mathematical tools with which to attack noise problems. Starting from the basic notion of Fourier series he leads in a simple manner to the idea of Fourier integral and transform. He also introduces the concept of power spectrum and its relationship to autocorrelation function. The chapter on probability covers the principles of this subject, giving insight into the idea of variate space and leading from the notion of discrete probabilities to that of a continuous probability density.

The main text starts with a definition of random processes. Mention is made of the properties of

stationary and ergodic processes, illustrating them by means of suitable examples. In fact, one of the great virtues of the book from the point of view of the student approaching the subject in complete ignorance is the large number and relevance of the illustrative examples.

These principles are applied to the derivation of a number of fundamental circuit aspects of noise; derivations which, perhaps in an over-zealous attempt to be straightforward, become rather laboured. The application to practical electrical devices gives a good insight into the noise behaviour of a number of physical devices, in the process of illustrating the application of the theory. This section is naturally far from exhaustive, and this point might have been better brought out if a wider variety of physical systems had been considered; the only devices mentioned are thermionic valves; no mention is made of noise in transistors or other solid-state devices. The section dealing with measurement of noise is, unfortunately, far too brief to do justice to the topic, but as this is essentially a theoretical book this is not of major importance.

The book develops with further theorems related to noise figures and the calculation of optimum arrangements for minimizing them. The reason for this is fully explained in the following chapter which, in great detail, enunciates the problem of detecting ever smaller signals in the presence of noise, stressing the close connexion between accuracy and time taken for an observation.

The remaining section of the book deals with the theoretical aspects of the characteristic function, leading to an analysis of the detection of alternating signals in the presence of noise by means of a non-linear detecting element.

The reason for the final chapter in the book, dealing with target noise, is seen in the author's personal interest in this field. As a consequence, its irrelevant inclusion in a book dealing primarily with the fundamental theory of noise may be excused.

The book thus well comes up to the author's aim of providing a simple introduction to the techniques of noise calculation. From this point of view it is probably the best book yet available for the student and yet one which will be valuable for reference at a later date.

R. A. King

CONVEX GEOMETRY

Convexity

By Dr. H. G. Eggleston. (Cambridge Tracts in Mathematics and Mathematical Physics.) Pp. viii + 136. (Cambridge: At the University Press, 1958.) 21*s*. net.

Problems in Euclidean Space

Application of Convexity. By Dr. H. G. Eggleston. (The Adams Prize Essay of the University of Cambridge, 1955–6.) (International Series of Monographs on Pure and Applied Mathematics, Vol. 5.) Pp. viii + 165. (London and New York: Pergamon Press, 1957.) 40*s*. net.

THE basic concept of convexity is simple but powerful. For example, given an ordinary function the graph of which is convex, so that any arc is below its chord, if arbitrary positive masses are attached to a finite number of points, the centroid of such masses is obviously above the curve; but this almost trivial observation can be made to yield most of the significant elementary inequalities of analysis, such as the Cauchy–Hölder inequality. Again, a set of points is convex if, when A and B belong to the set, so do all the points of the straight line segment AB. Since many elementary geometrical figures are convex, the question of the relation of convexity to properties of such figures at once arises, leading, for example, to the curious and important notion of curves of constant width.

Dr. H. G. Eggleston's two books are complementary. In the Cambridge Tract, the object is to develop the general theory of convexity, for its own sake, in n-dimensional Euclidean space; in the Pergamon Press volume, which consists of the Adams Prize Essay in the University of Cambridge for 1955–56, convexity is the thread connecting a variety of geometrical problems in Euclidean space of two or three dimensions.

A natural description of a plane convex set would be that it lies wholly on one side of any tangent to its boundary, but this is too restrictive (it would rule out a triangle); more generally and more precisely, through every point on the boundary of a convex set there passes a line which does not intersect the set. This provides a convenient and powerful alternative definition of convexity, once its equivalence to the earlier definition is established. Two other valuable tools are the relation between convex sets and convex functions, and Blaschke's selection theorem, which asserts that an infinite aggregate of closed convex sets in a bounded space must contain a sequence converging to a limit set which is closed, convex and not vacuous. All this basic theory is developed for n-space in the first four chapters of the Cambridge Tract. The fifth chapter concerns Minkowski's definition of surface area (the volume is simply the appropriate Lebesgue measure); this is a somewhat difficult chapter, for the motivation will scarcely be clear to the general reader. The final two chapters deal with typical geometrical problems: isoperimetrical properties and curves of constant width.

The second book is divided into four sections. In the first, convexity is merely a tool for the investigation of results in point-set theory; in the second, Borsuk's conjecture that any set of diameter d in n-space is the union (sum) of $n + 1$ sets each of diameter less than d is proved for 3-space by reducing the problem to one concerning convex sets. The third section deals with problems in which convexity appears as a natural restriction on the class of sets involved, such as the measure of closeness of approximation to a convex set by a convex polygon. Finally, special problems about plane convex sets are considered: sets of constant width, and inequalities connecting a plane convex set and its circumscribing triangles.

Dr. Eggleston's exposition is patient and thorough. But the book is for the specialist rather than for the general mathematical reader. Proofs are inevitably long, because of much complicated detail and some tedious but necessary enumeration of cases. Even the author's craftsmanship cannot always cut clearly through the tangle of detail. But there are many unsolved problems in this field, and the young research worker who has a taste for this type of patient analysis will find Dr. Eggleston's books invaluable, both as an account of the present state of knowledge and as a guide to likely lines of advance.

T. A. A. Broadbent

RADIOACTIVITY DUE TO FISSION PRODUCTS IN BIOLOGICAL MATERIAL

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THE release of artificial radioactive products into the biosphere has raised the problem of determining whether or not the resulting increase in the radioactivity of the environment represents a potential hazard to human beings. In attempting to assess any possible hazard, the first necessity is to obtain accurate, detailed information on the nature and amounts of radionuclides, both natural and artificial, occurring in the environment and the human body. Difficult problems arise in these studies of artificial radionuclides, and elaborate techniques are needed for distinguishing them from naturally occurring radioactive species. In Great Britain admirable investigations have been made by the United Kingdom Atomic Energy Authority[1-3]. However, in order to obtain independent information we have undertaken studies of beta- and gamma-emitting fission-product radionuclides in biological materials (Table 1), the programme being linked with other investigations in this Department on natural alpha-emitters[5,6]. We outline below the methods we are using and our initial results for a series of samples of cows' milk and human milk. By a fortunate coincidence the most detailed part of our cows' milk sampling programme covered the week in which the accident occurred at the Windscale No. 1 pile, and the results therefore provide an interesting record of the levels of fission products in milk produced at that time in Cardiganshire, Wales.

Estimation by Chemical Separation and Beta-Counting

Several radionuclides may be present in a single biological sample, and the levels of artificial and naturally occurring radioactivity in the sample may be of the same order of magnitude. For this reason, and to concentrate the activity, a suitable chemical separation must be made before the sample is assayed by beta-counting. Identification of particular radionuclides should be supported by measurements of half-life, or of maximum beta-energy.

Table 1. Recent Data (ref. 4) for certain Fission Products

Nuclide	Half-life	Chief transitions: Beta: Max. energy (MeV.)	Chief transitions: Gamma: Energy (MeV.)	Chief transitions: Gamma: Quanta emitted per 100 disintegrations	Remarks
Sr-89	54 days	1·46*	—	No gamma	—
Sr-90	28 years	0·61*	—	No gamma	—
Y-90	65 hours	2·24*	—	No gamma	Product of Sr-90
I-131	8·05 days	0·61	0·364	83	—
			0·638	7·5	
Cs-137	30 years	0·52	—	No gamma	—
Ba-137m	2·60 min.	No beta	0·662*	82†	Product of Cs-137

* Sole transition.
† For 100 disintegrations of cæsium-137.

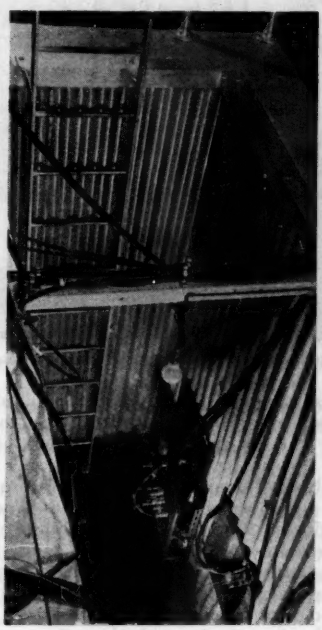

Fig. 1. Low-background pit for sample counting

The activities to be measured are, of course, frequently very small. Preliminary investigations showed that a beta-counting system, with a background of between 0·1 and 1·0 c.p.m. (counts per minute) and an efficiency of approximately 20 per cent, would be suitable for measurements on a wide range of samples. Assemblies were therefore constructed using end-window Geiger–Müller counters (G.E.C. Type *GM4 LB*), which have low natural backgrounds. The cosmic-ray background was reduced by the use of an anti-coincidence shield, incorporating 20 glass-wall cosmic-ray counters (20th Century Electronics, Type *G24*). To shield the whole assembly from external gamma-radiation, use was made of the chalk which forms the top rock stratum of our laboratory site, and is low in radioactive content. A pit 8 ft. × 3 ft. × 7 ft. deep, with five short galleries (Fig. 1), was excavated in the rock beneath a basement laboratory. The counter assemblies were set up in these galleries with additional shielding of 2 in. of 50-year-old lead. The background so obtained for a number of sample

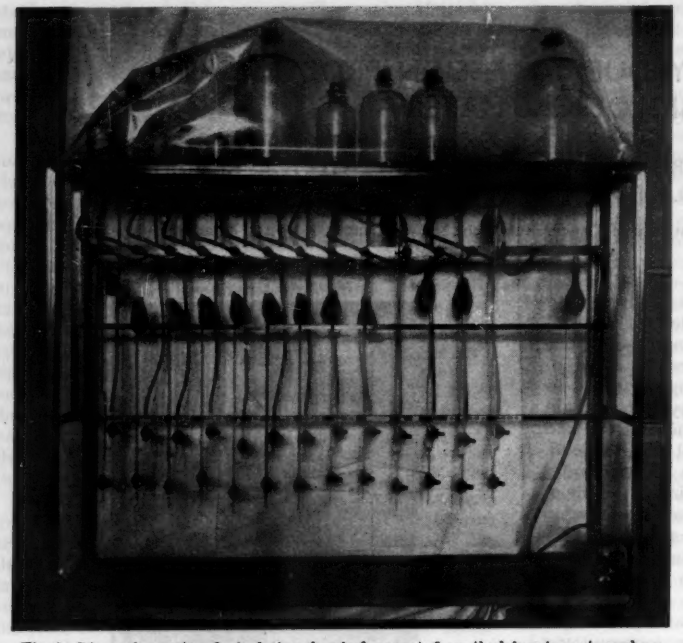

Fig. 2. Dispensing system for isolating chemical reagents from the laboratory atmosphere

counters has ranged from 0·4 to 0·6 c.p.m., individual counters showing variations from the mean not exceeding ± 0·05 c.p.m. over a period of several weeks.

The analysis of samples for radiostrontium involves the use of a number of chemical reagents and separation procedures. To reduce the possibility of obtaining false results due to radioactive contamination, several precautions were taken. Adequate stocks of prepared reagents, isolated from the atmosphere, were stored in a special dispensing system (Fig. 2). Provided that a control sample showed no measurable activity, it could be assumed that none would be introduced by the reagents during the ensuing series of estimations. The laboratories were quite separate from those used for normal radioactive tracer work, and access was strictly limited. We have collected a number of sealed samples of pre-1945 materials, including some of the foodstuffs recently recovered from the Scott/Shackleton stores in Antarctica. These fission-product-free materials have been used in periodic control runs, which have shown the reagents to be free from radioactive contamination at levels we can detect.

The radiochemical procedures used in the estimation of strontium-90 and strontium-89 were basically those described by Bryant *et al.*[7]. Milligram quantities of inactive strontium are added as carrier to ashed samples of biological materials, followed by chemical separation of the strontium from the mixture. Final scavenging with barium chromate and then ferric hydroxide removes trace amounts of natural series radionuclides and rare earth fission products that may be present. A small amount of inactive yttrium as carrier is then added to the strontium fraction and the solution stored for about two weeks while yttrium-90 builds up to nearly complete radioactive equilibrium with the parent strontium-90. Estimations of strontium-90 are based on measurements of the daughter yttrium-90 selectively precipitated as yttrium hydroxide and mounted for counting as oxalate. Estimations of strontium-89 are based on measurements of the strontium fraction precipitated as carbonate, allowance being made for strontium-90 and yttrium-90 in the precipitate.

The decay of yttrium-90 and strontium-89 fractions has always been followed. Typical results are shown in Fig. 3. In our experience measured half-lives agreed, within the limits set by counting errors, with the known values for these nuclides.

The end-window counters were calibrated individually for each of the nuclides studied. The stock solutions had been standardized in this laboratory (for strontium-90 plus yttrium-90 also at the National Physical Laboratory), by 4π beta-counting[8]. Dilutions, prepared gravimetrically, were treated chemically as described above to prepare sources of known activity for counting. As a further check on the accuracy of the calibrations, measurements were made on an international strontium-90 plus yttrium-90 milk ash standard, distributed by the United States Atomic Energy Commission Health and Safety Laboratory; our values were in good agreement with the mean of those of several other laboratories.

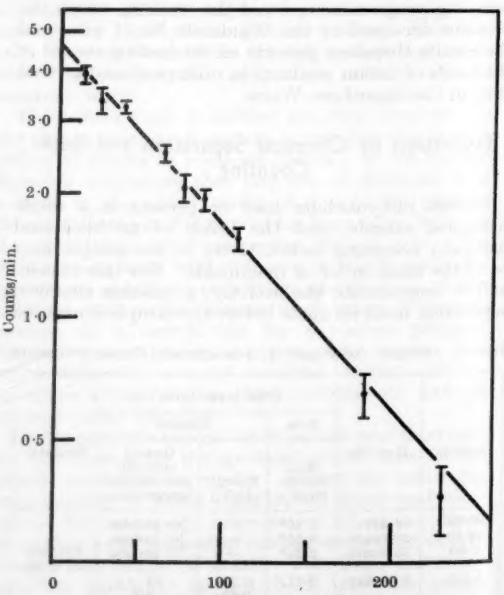

Fig. 3. Typical decay curve for yttrium-90 sample derived from cows' milk (sample *CMF* 1). The errors shown (2 σ) are based on the total number of counts measured for each point corrected for background. The curve is fitted by the method of least squares with due allowance for the weight of each measured value. Measured $T_{1/2}$ = 66·4 hr. (σ = 0·7). (cf. 65 hr., ref. 4)

Estimation by Gamma-Scintillation Spectrometry

In favourable cases gamma-emitting nuclides in biological samples may be identified and assayed by direct measurements using a sodium iodide gamma-scintillation spectrometer. This technique has the further advantage that comparatively large samples may be used, since self-absorption of gamma-radiation is small.

We have used two systems, each of which was carefully calibrated with standard sources prepared in a form simulating the samples to be assayed. In the first system a crystal 4 in. diameter × 2 in. high and photomultiplier, coupled through standard equipment to a single-channel pulse-height analyser, was set up in a gallery of the low background pit. A second, and improved system, was designed to have an inherent low background and high stability. A crystal 3 in. diameter × 3 in. high, with very low natural radioactive content (2–4 parts per million potassium), canned in electrolytic copper and having a quartz window, was used (Harshaw Chemical Co.). The associated photomultiplier has a stainless steel housing, and the whole detector is shielded by 16 in. of steel. The system is operated in conjunction with a 99-channel pulse-height analyser (A.E.R.E. Type 1438*B* and *C*) and has a total background above 100 keV. of 350 c.p.m. The capabilities of our equipment are illustrated by the ability to identify and measure as little as 20 μμc. of cæsium-137 in a human milk sample in measurements over a counting time of 36 hr.

Measurements on Cows' Milk

At the present time, the immediate sources carrying fission products into the human body are not fully known. It is clear, however, that in Great Britain milk is a principal source of strontium-90, the fission product causing greatest concern[9]. We therefore decided to make measurements of strontium-90 in milk in order to establish the average level for a well-defined area and to follow the general trend of levels with time.

Apart from the influence of fall-out rate, variations in the levels of fission products occurring in milk may be caused by numerous factors. For the proposed investigation, it was essential to obtain samples representative of a large quantity of milk so that fluctuations, reflecting special conditions at individual farms, would be smoothed out. By kind co-operation of the Milk Marketing Board we have arranged for a supply of spray-dried, skimmed-milk samples to be sent to us at weekly intervals from Felinfach Creamery, where up to 30,000 gallons of milk, drawn from more than 1,500 farms, are processed daily. The farms are located in an area of mixed coastal and upland herbage covering a few hundred square miles in west Cardiganshire. Each sample is a composite one, prepared from periodic samplings of the dried product made at half-hourly intervals throughout a given day. Four consecutive weekly samples are eventually bulked together, and it is proposed to measure the levels of strontium-90 in these bulked preparations over an extended period. In addition, the levels of other fission products, particularly strontium-89 and cæsium-137, are being followed.

As a preliminary investigation, in order to obtain information on the variations which might occur over short times, a series of daily samples was obtained covering October 5–13, 1957. During this period radioactive material was released into the atmosphere as a result of the accident at the Windscale No. 1 pile (October 10 and 11)[10]. Numerous measurements were made on the levels of activity in these daily samples and afterwards in samples produced at fortnightly intervals until December 1957, when the bulked series was commenced. The results of these measurements are shown in Fig. 4. In addition to the results shown in Fig. 4, measurements were made on three samples produced at the same creamery during 1956–57 (Table 2,*a*). The principal effects of the Windscale accident, discussed below, were temporary increases in the iodine-131 and cæsium-137 levels; no effect on the radiostrontium-levels was detected. The main features of the results for each nuclide studied are as follows:

Strontium-90. The main information on the levels of strontium-90 occurring in milk produced in Great Britain is that published by Bryant *et al.*[1,2]. The annual mean values found by these workers for a series of samples produced in Somerset during 1955 and 1956 were respectively 4·0 and 4·5 S.U. (1 S.U. = 1 μμc. ^{90}Sr/gm. calcium). Recently, they have reported a value of 5·1 S.U. (median) for 1957 for the same series[11]. Further measurements on samples produced during October and December 1956 at five other locations in Britain gave values ranging from 3·9 to 10·3 S.U., indicating a regional variation. Such variations have been discussed recently in terms of climatic and soil conditions[12].

The results obtained by us for Cardiganshire during 1956–57 are in close agreement with those of Bryant *et al.* for the same region and period (Table 2,*a*). Our later results, extending from October 1957 to May 1958 (mean value = 8·3 S.U.), show little change

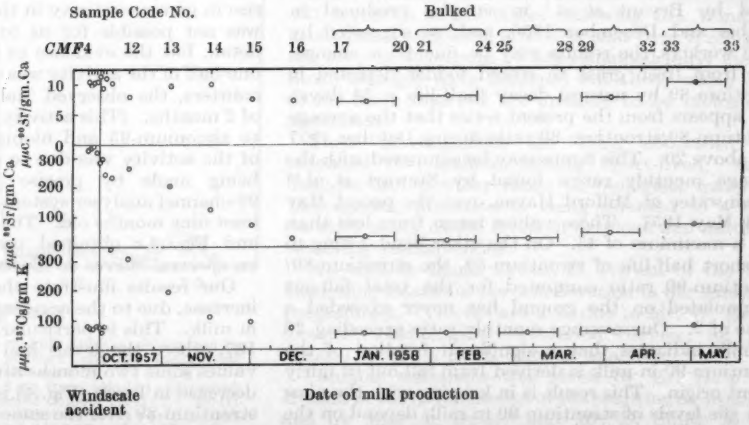

Fig. 4. Levels of fission products in cows' milk from west Cardiganshire, Wales, October 1957 to May 1958. All the values shown are accurate to within ± 10 per cent

Table 2. (*a*) Strontium-90 and Cæsium-137 Levels for pre-October 1957 Samples of Cows' Milk (Wales)

Sample	Date produced	Strontium-90		Cæsium-137		
		μμc./gm. Ca (S.U.)	μμc./litre liquid milk	μμc./kgm. dried skimmed milk	μμc./litre liquid milk	μμc./gm. K
(1)	(2)	(3)	(4)	(5)	(6)	(7)
CMF 1	April 1956	6·9	8·4	1,143	114	74
CMF 2	December 1956	8·4	10·2	1,102	110	71
CMF 3	January 1957	7·1	8·7	895	89	58
Bryant *et al.* (ref. 1)	October 1956	8·0				
	December 1956	7·2				
Bryant *et al.* (ref. 2)	April–August 1957 (mean value)	7·0				

Columns 3 and 5 directly estimated from measurements. Columns 4, 6 and 7 derived from columns 3 and 5 assuming that 1 litre liquid milk: (i) contains 1·22 gm. calcium and 1·54 gm. potassium; (ii) provides 100 gm. skimmed milk powder.

(*b*) Iodine-131 Levels for October 1957 Samples of Cows' Milk (Wales)

Sample	Date of milking	μμc./kgm. dried skimmed milk	μμc./litre liquid milk
(1)	(2)	(3)	(4)
CMF 9	10/10/57	$< 1 \times 10^3$	$< 1 \times 10^3$
CMF 10	11/10/57	$3{\cdot}8 \times 10^3$	$3{\cdot}8 \times 10^3$
CMF 11	13/10/57	77×10^3	77×10^3
CMF 12	19/10/57	32×10^3	32×10^3

Column 3 directly estimated from measurements; column 4 derived from column 3 assuming no loss in drying and same specific activity in whole and skimmed milk.

from the earlier values. Looking at Fig. 4,*a* it will be seen that neither during the week covering the Windscale accident, nor afterwards, was there any demonstrable increase in the strontium-90 content of the milk examined. The mean of the levels shown for October and November 1957 is 10·2 S.U., being slightly higher than the mean level of 7·6 S.U. for the subsequent months until April 1958. The value for May 1958 is again higher, 10·1 S.U., indicating a seasonal variation.

It will be seen that the levels found for strontium-90 in milk over the period 1955–58 have remained surprisingly steady. This suggests that the levels are not building up proportionately to the cumulative fall-out.

Strontium-89. The values for strontium-89 (Fig. 4,*b*) fall progressively from October 1957 until January 1958, the strontium-89/strontium-90 ratio decreasing from 30 to 4 over this period. Similar effects were found by Bryant *et al.*[1] in samples produced in October and December 1956, and, as suggested by these workers, the results may be due to a change-over from fresh grass to stored fodder depleted in strontium-89 by natural decay (half-life = 54 days).

It appears from the present series that the average strontium-89/strontium-90 ratio during October 1957 was above 20. This figure may be compared with the average monthly ratios found by Stewart *et al.*[13] in rainwater at Milford Haven over the period May 1954–May 1957. These values range from less than 1 to a maximum of 45. On the other hand, owing to the short half-life of strontium-89, the strontium-89/strontium-90 ratio computed for the total fall-out accumulated on the ground has never exceeded a value of 2. Our average monthly ratio exceeding 20 in milk indicates that a significant fraction of the strontium-90 in milk is derived from fall-out of fairly recent origin. This result is in keeping with the view that the levels of strontium-90 in milk depend on the rate of fall-out and do not rise in proportion to the cumulative fall-out.

Cæsium-137. The levels of cæsium-137, both in samples produced immediately before the Windscale accident and after December 1957, are close to those found in our three 1956 samples (Table 2,*a*). Similar values were obtained by Booker[3] for Welsh milk sampled in October 1956. Excluding the rise immediately after the Windscale accident these results follow the pattern for strontium-90, namely, that the levels due to fall-out have remained steady. It is interesting to note that, as for strontium-90, the levels of cæsium-137 in the present Cardiganshire series are approximately double those reported for Somerset during 1955–56[3].

Effect of the Windscale accident on the levels of cæsium-137 *and iodine*-131. The area from which the present series of samples is drawn is approximately 160 miles south-south-west of Windscale. At the time of the accident our arrangements for gamma-scintillation spectrometry were incomplete, but we were able to set up rapidly the single-channel system described above and to carry out measurements directly on dried milk samples (0·5–1 kgm.) a few days after the accident. This system was used for measuring the levels of iodine-131 in three samples produced shortly after the accident. This radionuclide was identified by observation of a peak appearing at 360 keV. combined with estimations of half-life. The results of these measurements are listed in Table 2,*b*. It will be seen that, although the cloud avoided north Wales[14], in south Wales some deposition occurred. Further measurements with the single-channel system demonstrated in samples produced immediately after the Windscale event a pronounced rise in gamma-activity in the 600–700 keV. band. It was not possible for us to analyse this activity in detail, but the evidence to hand suggests that about one-half of the activity was due to short-lived gamma-emitters, the observed 'half-life' being in the region of 2 months. (This activity is probably to be ascribed to zirconium-95 and niobium-95[15].) The remainder of the activity was due to cæsium-137, identification being made by precise measurements using the 99-channel analyser system when the samples were at least nine months old. The values shown in Table 2,*a* and Fig. 4,*c* obtained on this system are based on spectral curves as illustrated in Fig. 5,*b*.

Our results illustrate the transient nature of the increase, due to the accident, of the activity occurring in milk. This is particularly well shown for cæsium-137, where the levels had returned to pre-accident values some two months afterwards. The progressive decrease in levels (Fig. 4) is similar to that found for strontium-89 over the same period and may be related partly to the change-over in the cows' feed during winter. It is noteworthy that the cæsium-137 level

Table 3. Strontium-90, Strontium-89 and Cæsium-137 in Samples of Human Milk

Sample	Date collected	μμc. Strontium-90		μμc. Strontium-89		μμc. Cæsium-137		
		Per gm. Ca in ash (*a*)	Per litre liquid milk	Per gm. Ca in ash (*a*)	Per litre liquid milk	Per gm. ash (*b*)	Per gm. K in ash (*a*)	Per litre liquid milk
HM 1	Sept. 4–19, 1957	< 1·5	< 0·3	< 10	< 2	5·0	19	11·4
HM 2	Sept. 27–Oct. 11, 1957	< 0·5	< 0·2	< 5	< 2	4·0	21	9·9
HM 3	Oct. 15–28, 1957	—	—	—	—	4·6	21	10·3
HM 4	Oct. 12–20, 1957	—	—	—	—	4·9	20	9·4

(*a*) Calcium and potassium content measured for individual samples; (*b*) in our experience, less than 20 per cent of the total cæsium-137 present in milk is lost during ashing at 600° C.

for May 1958, although showing a slight rise above the winter values, is still close to the pre-accident level. This indicates that the activity released during the accident is no longer being incorporated in the grass.

The ratio of iodine-131 to cæsium-137 in our sample produced on October 13, 1957, was 20, lying between values reported for airborne activity on October 11 by Stewart *et al.*[14] (9·0) and Chamberlain *et al.*[15] (38·5). The increases in absolute levels in Cardiganshire were considerably smaller than those reported at Windscale. Thus, the iodine-131 value found by us on October 13 was less than 1 per cent of the highest level (1·4 μc./litre) found in the Windscale area (October 13, at a farm 10 miles from the works)[16]. There is little doubt, however, that the increases measured for Cardiganshire were a result of the accident and not a result of fall-out from distant bomb tests, which would have produced a corresponding increase in radiostrontium-levels.

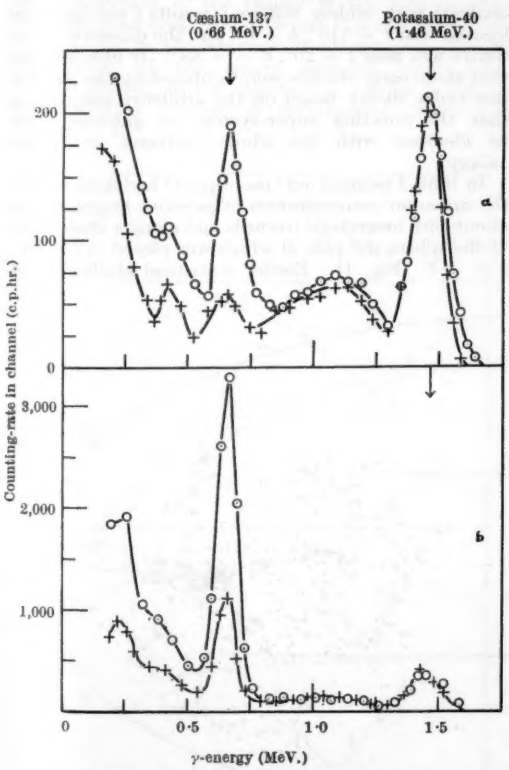

Fig. 5. Typical gamma-spectra of milk samples, determined in July 1958, using 99 channel analyser and low background (NaI(Tl)) crystal assembly.
(*a*) (i) Ashed cows' milk *OM* 8 15·5 gm. (pre-1945) (+); (ii) ashed human milk *HM* 3 13·3 gm. collected October 1957) (○). (*b*) (i) Dried cows' milk *CMF* 4 451 gm. (dried 6/10/57) (+); (ii) dried cows' milk *CMF* 12 420 gm. (dried 20/10/57) (○). (All spectra corrected for instrument background)

Measurements on Human Milk

We have made observations upon four samples of human milk, ranging in volume from 2·5 to 6 litres. Each sample was obtained from an individual donor and was collected over a period of a few weeks during September and November 1957. On receipt the milk was reduced to dryness and then to ash. Gamma-spectra were obtained for these ashed samples using the multichannel analyser, and in each case the photo-peak of cæsium-137 was found at 660 keV. A typical spectrum is shown in Fig. 5,*a*, in comparison with a spectrum obtained from a pre-1945 sample of cows' milk ash. Estimated activities in the samples are given in Table 3. Two of the samples were analysed for radiostrontium but it was not possible to detect any such activity. The values for strontium-90 and strontium-89 shown in Table 3 are upper limits based on the limiting sensitivity of the method.

We are not aware of previous measurements of cæsium-137 in human milk. The levels we have found (expressed as μμc./gm. potassium) are similar to those observed in cows' milk from Somerset[3] and about one-third of the values in our Cardiganshire series. It is interesting to note that these levels in human milk are very close to those reported by Rundo (20–48 μμc./gm. potassium)[17] for total body measurements on human subjects during 1956–57.

In summary, it will be seen that our measurements of the levels of activity of fission products in milk are, where comparable, in good agreement with those previously published. It was possible to detect a small transient increase of iodine-131 and cæsium-137 levels in south Wales following the Windscale accident. It appears, however, that over three years the level of strontium-90 has remained fairly steady. Small changes have occurred but those which have so far been observed are unlikely to be biologically significant.

These investigations are being continued and extended to include other, short-lived, radionuclides and a wider range of biological materials. Throughout, attention is being directed to a comparative study of the levels of artificial and naturally occurring radionuclides.

We wish to thank Dr. A. L. Provan of the Milk Marketing Board for his collaboration in our sampling programmes. Thanks are also due to Mr. W. Binks, director, Radiological Protection Service, for permission to use a multi-channel analyser.

Valuable assistance was given by Mr. H. J. D. Ireland in the development of the counting equipment, and by Miss A. Dulley and Mr. D. Smith in the estimations.

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THE LOCAL SUPERCLUSTER OF GALAXIES

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Harvard College Observatory, Cambridge, Massachusetts

IN 1946, G. Gamow[1] advanced the speculative hypothesis that, possibly, " . . . the realm of galaxies . . . represents only a small part of a much larger system (a 'super-galaxy' in the super-Shapley sense) rotating around a distant centre", perhaps " . . . located far beyond the reach of our telescopes". As a test of this hypothesis, he suggested a search for a double-sine periodicity, similar to the Oort effect of stellar radial velocities in the Galaxy, in the radial velocities of external galaxies.

In 1951, Mrs. V. Cooper-Rubin[2] analysed the available velocities of about one hundred galaxies and found evidence for such an effect; the expected alternation of positive and negative residual velocities (after correction for solar motion and a linear red shift) was best displayed along a great circle of the sphere the pole of which was located at galactic co-ordinates $l = 14°$, $b = +10°$. This was taken to define a 'universal' plane of rotation, and tentative rotational constants were derived for the 'universe'. The direction of the centre was placed near $l = 104°$, $b = +5°$ or 180° from this position.

In 1952, K. F. Ogorodnikov[3] carried out a similar analysis with widely different results: the pole was located near $l = 110°$, $b = 0°$, and the direction of the centre was near $l = 20°$, $b = +88°$. It now appears that these early studies were confused by the use of a first-order theory based on the arbitrary assumption that the rotating super-system of galaxies must be identical with the whole 'universe' or 'meta-galaxy'.

In 1953, I pointed out[4] (as others[5,6] had done before) the apparent concentration of galaxies brighter than about 15th magnitude towards and along a great circle of the sphere the pole of which was placed at $l = 15°$, $b = +5°$ (Fig. 1). Earlier statistical studies[7,8] had

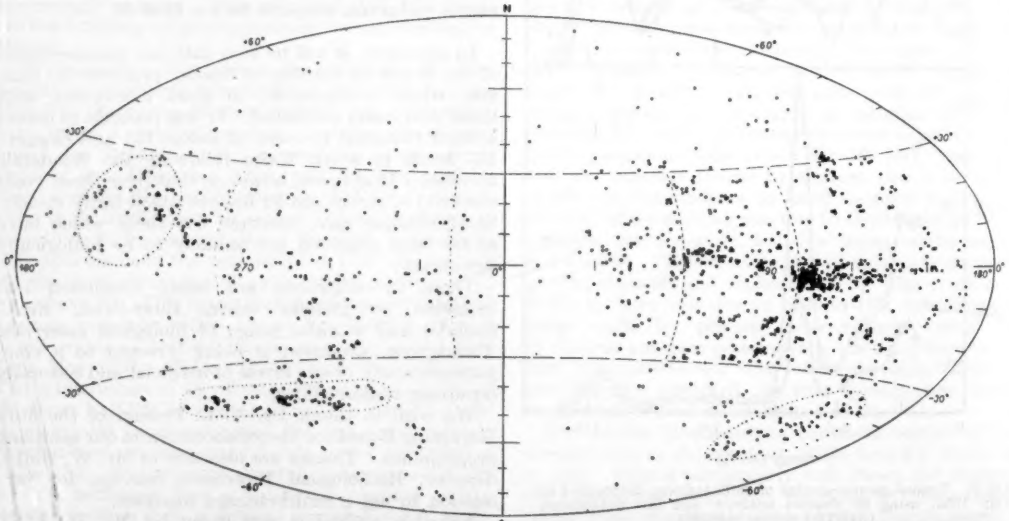

Fig. 1. Distribution in supergalactic co-ordinates of the brighter galaxies ($8{\cdot}0 \leq m_{pg} \leq 12{\cdot}9$). The northern galactic hemisphere is to the right; galaxies of known velocity are denoted by filled circles; those of unknown velocity, by open circles. Note that the majority of the galaxies lie between latitudes ± 30°. Three probable external supersystems are outlined by dots. The two critical longitude sectors discussed in the text are delimited by short dashes

indicated the presence of a large 'metagalactic' cluster or supercluster in our neighbourhood with a centre in the general direction of the north galactic pole, but they had received little attention. I therefore suggested that this 'Milky Way' of galaxies is the trace of a local super-system of clouds and clusters of galaxies—a local Supergalaxy—within which the local group of galaxies (including our own) is located, rather far away from a centre placed in or near the great Virgo cluster of galaxies at $l = 255°$, $b = +75°$.

Further study[9] indicated an overall diameter of 6–8 megaparsecs on the old (1936) distance scale, corresponding to about 30 megaparsecs on the current scale. The distance of the Virgo cluster is 10–13 megaparsecs in this revised scale.

The strong flattening of the system (axial ratio 1 to 5) was from the beginning[4,9] taken as supporting evidence for the hypothesis of a general rotation. Rotation, in fact, constitutes the critical test of the reality of the super-system as a physical unit held together by its self-gravitation; for in the absence of rotation the singular distribution of the nearer galaxies would have to be regarded as not significant, merely a chance grouping of a number of independent clouds and clusters.

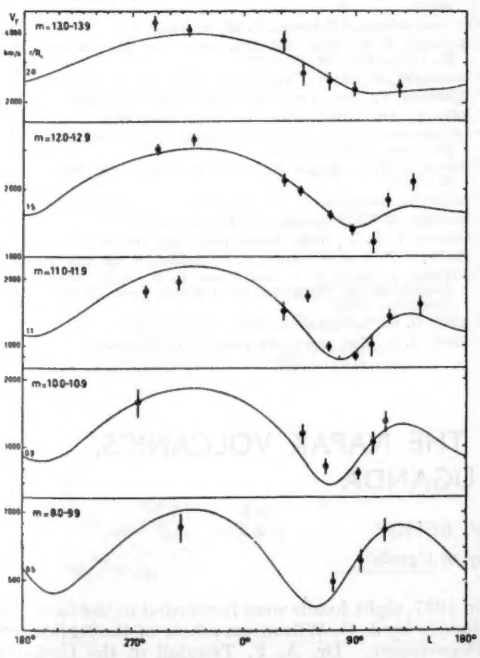

Fig. 2. Mean radial velocities of galaxies brighter than the 14th magnitude as a function of supergalactic longitude. The mean points with their probable errors refer to more than 300 galaxies within ± 30° of the supergalactic equator. The theoretical curves are computed from the model described in the text

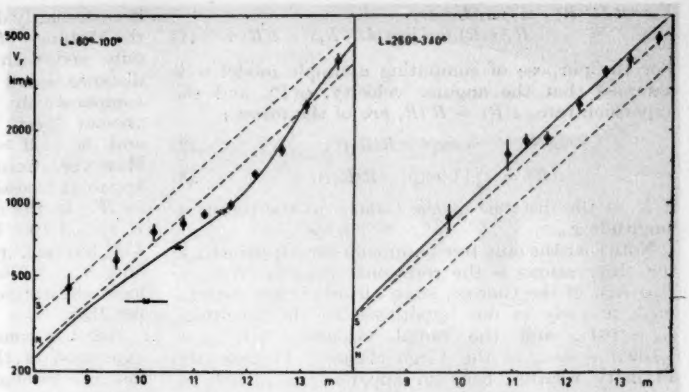

Fig. 3. Mean radial velocities of galaxies in the supergalactic equatorial belt as a function of magnitude in two longitude sectors. The theoretical curves are computed from the model described in the text. The dashed lines are the solutions for uniform expansion in the northern and the southern galactic hemispheres, according to Sandage. The crosses (left) give the mean magnitude $\bar{m}(V_r)$ in three velocity ranges to illustrate regression effects

A critical check has become possible through the publication in 1956 of the Lick – Mt. Wilson – Palomar general catalogue of radial velocities of galaxies[10]. Fig. 2 and Fig. 3 show the main results of an analysis of the radial velocities of more than 300 galaxies brighter than the 14th magnitude and located within 30° of the supergalactic equator.

In Fig. 2 the mean radial velocities are plotted as a function of supergalactic longitude L for 5 intervals of apparent magnitude. The mean points disclose a conspicuous, systematic longitude effect which, at small distances (small m), approximates the double-sine wave expected in a system in differential rotation.

In Fig. 3 the mean radial velocities are plotted against apparent magnitude for two critical longitude sectors. In the sector $260° \leqslant L \leqslant 340°$, corresponding to the supergalactic anti-centre sector (and to the southern galactic hemisphere), the relation between $\log V_r$ and m is approximately linear; in the other sector, $60° \leqslant L \leqslant 100°$ (near the north galactic pole), the non-linearity is conspicuous; further, the mean velocities at a given apparent magnitude (hence, at a given distance) are widely different in the two sectors.

This discrepancy had already been noted by Sandage[10] as a puzzling effect detracting from the usual assumption of isotropy. The conclusion seems inevitable that, contrary to orthodox theory, the red shift is neither linear nor isotropic among the brighter galaxies; the results are, however, consistent with and easily interpreted by the Supergalaxy hypothesis.

We assume that the local supercluster is in a state of differential rotation and differential expansion about its centre in the Virgo cluster. The first assumption does not require amplification; the second, which accounts for the north-south asymmetry, is made the more plausible by a variety of theoretical and empirical arguments suggesting that in condensed regions of space (groups, clusters) the expansion rate is reduced locally by gravitational attraction; for example, the Galaxy and the local group are probably not expanding. On these assumptions, the radial velocity of a galaxy in longitude L at distance r from us, and R from the centre of rotation, is given by the classical relation:

$$V_r = R_1[\omega(R)-\omega_1]\sin(L-L_0) - R_1[\varepsilon(R)-\varepsilon_1]\cos(L-L_0) + \varepsilon(R)\cdot r \quad (1)$$

For the purpose of computing a simple model it is assumed that the angular velocity, $\omega(R)$, and the expansion-rate, $\varepsilon(R) = R'/R$, are of the forms:

$$\omega(R) = \omega_0 \exp(-R/R_1)^2 \quad (2)$$

$$\varepsilon(R) = \varepsilon_\infty[1-\exp(-R/R_1)] \quad (3)$$

if R_1 is the distance of the Galaxy to the centre in longitude L_0.

Note that the only free parameter for adjustment to the observations is the rotational velocity, $R_1\omega_1 = R_1\omega(R_1)$, of the Galaxy, since all others are determined uniquely in our hypothesis by the longitude, $L_0 = 104°$, and the radial velocity, $\varepsilon_1 R_1 = +1{,}100$ km./sec., of the Virgo cluster. Further, the auxiliary relation between apparent magnitude m and distance r is also given by the Virgo cluster where $\overline{m} = 11{\cdot}5$ at $r = R_1$.

As shown by the computed curves in Figs. 2 and 3, excellent agreement is obtained if $\omega_1 R_1 = 500$ km./sec. (with an estimated probable error of $\pm$ 50 km./sec. The values of r/R_1 range from 0·5 to 2·0 as m increases from 8–9 to 13–14; this large range makes it clear why a first-order theory is inapplicable, quite apart from the complication of the non-linear expansion.

From the rotational velocity we derive the total mass of the supersystem, $M(\text{tot.}) \approx 10^{15}$ solar masses (assuming a modulus $m_0 - M = 30{\cdot}0$, $R_1 = 10$ Mpc.). This appears to be a reasonable value when compared with estimates of the mass of the Virgo cluster, $M(\text{nucleus}) \approx 10^{14}$ solar masses, based on velocity dispersion[16].

This analysis supports the conclusion that the local supercluster of galaxies is an irregular assembly of groups, clouds and clusters dominated by the Virgo cluster in its centre, and that it has reached at least some degree of dynamical equilibrium involving rotation, expansion, and random motions. The Galaxy partakes in the slow general rotation of the system with a velocity of the order of 500 km./sec. directed towards $L = 194°$ ($l = 287°$, $b = -14°$). The present or 'instantaneous' period of revolution is of the order of 5×10^{10} years near the centre, and from 10 to 20×10^{10} years in the outer regions.

The presence of differential expansion in the local super-system has an important consequence for the calibration of the law of red shifts, namely, the derivation of Hubble's expansion parameter, $H = V_r/r$. This is customarily done simply by dividing the velocity by the distance of the Virgo cluster, because it is the only one with both a significant red-shift and a distance small enough to be within the range of comparatively reliable distance indicators; with present 'best' estimates[13], $V_r = +1{,}136$ km./sec., and $m - M = 30{\cdot}7$, $H = 83$ km./sec. per Mpc. However, from equation (3), it follows that the apparent recession-rate of the Virgo cluster is $\varepsilon_1 < \varepsilon_\infty = H$. In the model above, $\varepsilon_1 = 0{\cdot}632\varepsilon_\infty$, so that if $R_1\varepsilon_1 = 1{,}100$ km./sec. and $R_1 = 10$ Mpc., $\varepsilon_\infty = 174$ km./sec. per Mpc.; if $R_1\varepsilon_1 = 1{,}136$ km./sec. and $R_1 = 12{\cdot}6$ Mpc. (modulus 30·7 less 0·2 mag. local absorption correction), $\varepsilon_\infty = H \approx 140$ km./sec. per Mpc.

Another consequence of differential rotation and expansion is that, in deriving the mean absolute magnitudes of galaxies from residuals of the velocity – magnitude relation, it is necessary to take account of the non-linearity and anisotropy of the velocity field. Details will be published shortly in the *Astronomical Journal*.

Although the philosophical notion of second-order clustering is an old one[18], the general existence of super-clusters of galaxies has only recently been demonstrated (and it is not yet universally accepted), mainly through the statistical analysis of counts of faint galaxies at Lick[14,15] and of clusters of galaxies at Palomar[16]. G. Abell[17] has recently reported preliminary estimates of the average size of some distant super-clusters which (on the same distance scale) agree well with the estimated diameter of the local supercluster.

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MIOCENE MAMMALIA FROM THE NAPAK VOLCANICS, KARAMOJA, UGANDA

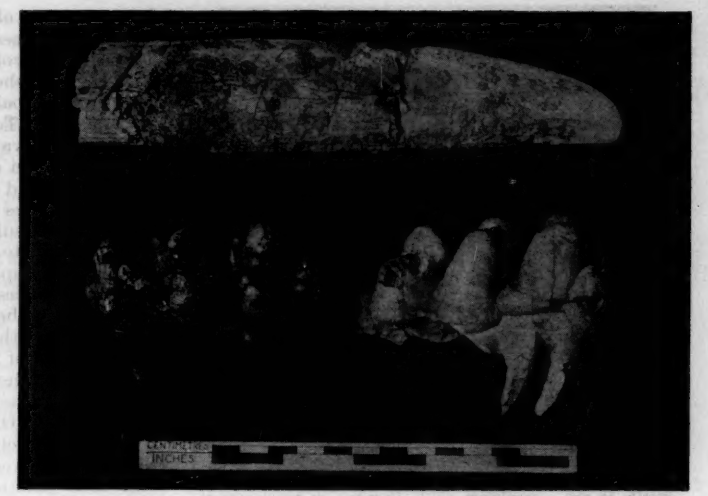
By Dr. W. W. BISHOP

Geological Survey of Uganda

THE mountain mass of Napak in Karamoja District, north-east Uganda (2° 5′ N., 34° 17′ E.) is the dissected remnant of a Tertiary volcanic cone in the group that includes Elgon, Kadam, Moroto and Toror (Fig. 1).

Mammalia were recorded from Napak as early as 1920 by E. J. Wayland but were not identifiable[1]. In 1957, eight fossils were forwarded to the Geological Survey by J. G. Wilson, an officer of the Agricultural Department. Dr. A. F. Trendall of the Geological Survey reported that detailed work might prove rewarding and as Wilson's specimens included a shattered proboscidean molar and a well-preserved rodent skull I went to the area early in 1958.

Three fossiliferous localities have been located but only the main site is described here. This is situated at a radial distance of six miles south-west of the carbonatite and ijolite plug which marks the position of the central vent. The fossiliferous beds are a series 100 ft. in thickness of horizontally bedded, unconsolidated fine grey tuffs with occasional agglomerate bands. The beds overlie a lava and thick coarse agglomerate and are in turn overlain by further agglomerate. The base of the fossiliferous series occurs at a height of 4,480 ft. O.D. and is 500 ft. above the basement rocks at this point. The beds are of only limited extent and owe their origin to the existence of a subsidiary vent, now represented by an agglomerate plug, which blocked a shallow valley on the flanks of the main volcano. Into the hollow so formed, fine detritus was washed, and ash and agglomerate were deposited by minor outbursts of activity. The hollow may have held water for short periods after heavy rainfall.



Photograph : Uganda Museum

Fig. 2. Molars and tusk of *Trilophodon angustidens*

Local non-sequences and reddened surfaces, the occurrence of abundant fossil wood and the presence of layers of calcareous nodules (kunkar), flags with rain-spotting, and layers of curled, sun-dried mudstone, give evidence of numerous breaks in deposition. The fossils occur sparingly upon these temporary land surfaces.

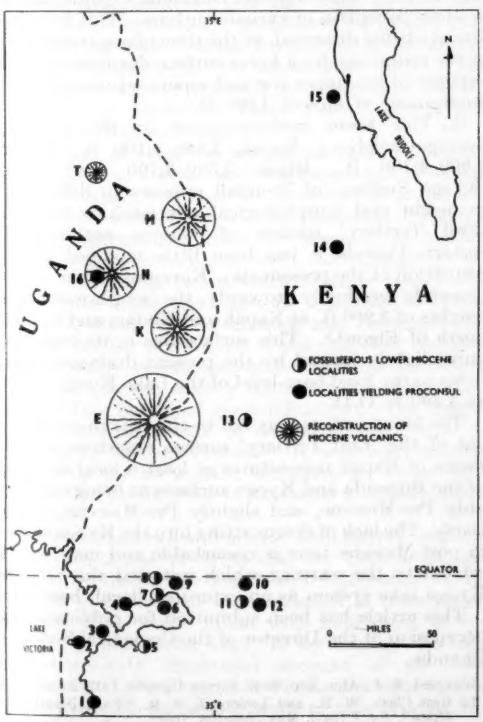


Fig. 1. Distribution of fossiliferous Lower Miocene deposits and the genus *Proconsul*. 1, Karungu; 2, Mfwangano; 3, Rusinga; 4, Uyoma; 5, Homa; 6, Maboko; 7, Majiwa; 8, Mariwa; 9, Ombo; 10, Songhor; 11, Muhoroni; 12, Koru; 13, Suk escarpment; 14, Loperot; 15, Losodok; 16, Napak; *E*, Elgon; *K*, Kadam; *N*, Napak; *M*, Moroto; *T*, Toror

To date the site has yielded 1,114 mammalian fossils. Of these, 778 are unidentifiable fragments of bone and tusk, many of which show marks of the teeth of carnivores. The remaining 336 pieces are made up as follows: 39 fragments of proboscidean teeth, including four well-preserved molars, and 45 fragments of tusk (Fig. 2); 35 pieces of rodent skull, jaw and teeth; 29 fragments of skull, jaw and teeth of various Primates, Carnivora, Artiodactyla and Perissodactyla; and 188 bones with distinct facets or form which are probably identifiable.

From a preliminary examination the following mammalia have been tentatively listed as occurring; *Proconsul nyanzae* (Le Gros Clark and Leakey); *Limnopithecus* sp.; Lemuroidea; Histricomorpha; Pedetidae; Anomaluroidea; *Pterodon* sp.; *Amphicyon* sp.; Carnivora; Suidae; Tragulidae; Chalicotheriidae; *Trilophodon angustidens* var. *kisumuensis* (Macinnes); Gastropoda (indet.); abundant fossil wood and occasional leaf impressions.

I am indebted to Mrs. S. Coryndon and to my wife for help with identification, and to Dr. L. S. B. Leakey, curator of the Coryndon Museum, Nairobi, for permission to study comparative material from Kenya and for the following note.

"I have made a preliminary examination of the better preserved fossils found by Dr. Bishop and they are of exceptional interest. Although the collection is small it includes enough typical forms to leave no doubt as to its affinities with the Lower Miocene faunas from Rusinga, Mfwangano, Songhor, Koru and the Lake Rudolf areas of Kenya.

"Of special interest is the presence of *Proconsul nyanzae* and the genus *Limnopithecus*. The former is represented by a very beautifully preserved and quite typical lower right second molar (Fig. 3) while the latter is part of the mandible in which the preservation is less good. There is no doubt that it represents the genus *Limnopithecus* and is probably referable to the species *legetet* but without a better specimen this cannot be stated with certainty."

Fig. 3. Lower right second molar of *Proconsul nyanzae*. Maximum length, 12 mm.; maximum width, 10 mm.; posterior edge of tooth at bottom of photograph. Photograph: L. S. B. Leakey

The quantitative analysis of the fauna reveals several points of interest. The action of carnivores as scavengers is seen in the numerous chewed bones and also in that 13 per cent of the fragments surviving as fossils are comparatively inedible teeth and jaws. The specimens are invariably broken or chewed before incorporation in the tuff and are never found as associated skeletons. This suggests that the animals died from natural causes or as a result of the action of predators and were not overcome by gases or ejected material during active periods of the volcano.

The most abundant group numerically were the Rodentia, which account for 23 per cent of all the teeth, jaws and skull fragments recovered. An abundance of rodents is also characteristic of the Kenya Lower Miocene.

The occurrence of fossil wood confirms that the non-sequences in the tuff represent periods when the lower slopes of the volcano became clothed temporarily with vegetation and provided a suitable habitat for the Hominoidea, Lemuroidea and Anomaluroidea.

The genus *Proconsul* is now known from ten major localities in western Kenya but this is the first record from Uganda. The distribution of the main localities yielding *Proconsul* together with the principal outcrops of fossiliferous Lower Miocene deposits is shown in Fig. 1.

The Napak material has been submitted to specialists for specific identification, and a full account of the fauna, stratigraphy and geomorphology of the site will be published at a later date. However, there seems little doubt of the similarity between the assemblage and the extensive faunas obtained from the numerous sites in the Kavirondo area of Kenya, 145–170 miles south of Napak. This material, with certain reservations, is at present considered to be of Lower Miocene Age and is equated with the European Burdigalian[2].

The Napak fossils occur in a simple stratigraphical context in a single volcano resting upon extensive peneplained surfaces developed upon steeply dipping Basement Complex rocks. Thus the deposits have a geomorphological importance in their relationship to former erosion-levels which is absent in the Kenya deposits, where large-scale rift movements and local faulting have frequently disturbed the Lower Miocene deposits and obscured their relationship to pre-volcanic surfaces. The importance of the faunal dating of the volcanics is threefold:

1. It establishes a Lower Miocene age for the early activity at Napak and possibly also at the associated volcanoes of Toror, Moroto, Kadam and Elgon. Despite their varying degrees of erosion these have previously been considered as broadly contemporary with Napak and of Pliocene age[3,4].

2. It provides an approximate morphological time-scale for the building up of the predominantly ash and agglomerate cone to about 10,000 feet above the Basement Complex[3], and its subsequent erosion to the present series of isolated hill remnants.

3. It dates the sub-volcanic surfaces of Napak and probably also those beneath Toror, Moroto, Kadam and Elgon as of Pre-Miocene age. It is possible that the more advanced erosion of Napak and Toror may indicate a rather earlier origin than Elgon, Moroto and Kadam. However, I agree with Trendall[5] that it is more likely that the degree of dissection is related to differences in original bulk of the volcanoes and their position in relation to the base-level of erosion and to major watersheds. Their approximate contemporaneity is supported by the similarity in height and form of the basement surfaces beneath Napak, with those of Moroto, Kadam and Elgon. Two major erosion-levels appear to be represented:

(*a*) An upper surface with the following average heights: Moroto 4,900 ft.; Napak 4,900 ft., Kadam 4,900–5,000 ft., Elgon 5,400–6,000 ft.[5–7], which appears to be the equivalent of the Pre-Miocene, Mid-Tertiary, Mid-Miocene, Buganda, Uganda, Middle or Main peneplain of various authors. This level was already being dissected, at the time of commencement of the eruptions, by a lower surface developing at the expense of the upper one and separated from it by an escarpment of almost 1,000 ft.

(*b*) This lower surface occurs at the following average heights: Napak 3,800–4,100 ft., Kadam 3,900–4,100 ft., Elgon 3,500–3,700 ft.[4,5]. This 'Kyoga Surface' of Trendall appears to differ little in height and morphological relationships from the 'End Tertiary' surface of various authors. In eastern Uganda it has been little modified by the formation of the present-day 'Karamoja Plain', which descends gradually towards the south-west from heights of 3,900 ft. at Napak and Kadam and 3,600 ft. north of Elgon[4,5]. This surface has in its turn been only slightly incised by the present drainage, which flows to the local base-level of the Lake Kyoga system at 3,400 ft. O.D.

The lower surface may not be the true time equivalent of the 'End Tertiary' surface elsewhere but the fauna of Napak necessitates at least a local re-dating of the Buganda and Kyoga surfaces as being considerably Pre-Miocene, and slightly Pre-Miocene, respectively. The lack of downcutting into the Kyoga surface in post-Miocene time is remarkable and may well be related to the warping which initiated the Victoria-Kyoga lake system as an extensive 'local' base-level.

This article has been submitted for publication by permission of the Director of the Geological Survey of Uganda.

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OBITUARIES

Prof. James Ritchie, C.B.E.

BORN in 1882 at Port Elphinstone, Aberdeenshire, the son of the local schoolmaster, James Ritchie, emeritus professor of natural history in the University of Edinburgh and president of the Royal Society of Edinburgh, died suddenly in Edinburgh on October 19 at the age of seventy-six. He had a notable career. Educated at Gordon's College and then at the University of Aberdeen, he joined the staff of the Natural History Department of the Royal Scottish Museum in 1907. Assistant keeper in 1919, he succeeded Dr. Eagle Clarke as keeper of the Department in 1921, but nine years later was appointed to the regius chair of natural history in the University of Aberdeen, following Sir J. Arthur Thomson, under whom he had been trained. In 1936 he returned to Edinburgh as professor of natural history, retiring in 1952. He was elected president of the Royal Society of Edinburgh in 1954.

It was highly fitting that the posts James Ritchie occupied were all designated, as largely remains the custom in Scotland, 'natural history'. He was, above all else, a naturalist, and no one had a better knowledge of the fauna of his country, both in the present and in the past, and more concern for its future. He published extensively and over an exceptionally wide field, ranging from marine hydroids and polyzoans to birds and mammals, and also made notable contributions to archæology, an interest he gained from his father, an earlier James Ritchie and a well-known amateur archæologist. He wrote three books, "The Influence of Man on Animal Life in Scotland" (1920), "Beasts and Birds as Farm Pests" (1931) and "Design in Nature" (1937).

The first of these represents his major contribution—and it is a great one—to knowledge of animal life in Scotland. It may be described as a work of scholarship written by a born naturalist. Ritchie had the advantage, which he stressed, of dealing with a small country and with the changes in the purely post-glacial fauna which neolithic man found when, some 9,000 years ago, he followed the northward migration of these animals into Scotland. He had the further advantage of the recorded observations of many generations of Scottish naturalists, of whom he was the worthy successor and ideal interpreter. This book had great influence on the growth of the youthful science of animal ecology, with its applications in conservation. It won international recognition for its author, including an award of a silver medal by the Société Nationale d'Acclimatation de France.

His investigations and advice were largely responsible for measures of protection for both seals and birds in Scotland. He found, by examination of the contents of caves near Inchnadamph in Sutherland, evidence of an arctic fauna with indications of the presence of palæolithic man. In archæology, his long and extensively illustrated account of the lake dwellings in Loch Treig is a classic description, and he was engaged on further work of this type at the time of his death.

Ritchie's activities were as wide as his interests. From its first inception in 1909, he took a great part in the development of the Royal Scottish Zoological Society, of which he became vice-president; he was secretary and later president of the Royal Physical Society; vice-president of the Scottish Marine Biological Association; chairman of the Council of the Royal Scottish Geographical Society; president of Section *D* (Zoology) of the British Association in 1939. He was for fourteen years editor of the *Scottish Naturalist* and was the natural choice as chairman of the Scottish Wild Life Conservation Committee which prepared the way for the establishment of the Scottish Committee of the Nature Conservancy, of which he was an initial member. Elected to the Royal Society of Edinburgh in 1916, he served many times on its Council, being secretary, later a vice-president and finally, in 1954, president. He was awarded the Keith Prize of the Royal Society of Edinburgh in 1944, was created C.B.E. in 1948 and received the honorary doctorate of laws from his own University of Aberdeen in 1952.

By his writings, his lectures to university students and to a wider public, and by his charming water-colour paintings of the Scottish landscape, James Ritchie was widely known, and his loss will be felt far beyond the circle of his friends and colleagues. He married Miss Jessie J. Elliot, who died in 1933, and is survived by his son, Prof. A. E. Ritchie, Chandos professor of physiology in the University of St. Andrews, and by his two daughters.

C. M. YONGE

Dr. T. A. Sprague

DR. THOMAS ARCHIBALD SPRAGUE, well known as a taxonomic botanist and an authority on plant nomenclature, died at his home in Cheltenham on October 22, at the age of eighty-one

He took the degree of B.Sc. at Edinburgh, under Prof. Bayley Balfour. In 1898, he undertook, with Captain H. W. Dowding, R.N., an expedition to Venezuela and Colombia, and the first set of the plants he collected are at Kew. Sprague was appointed to the staff of the Herbarium of the Royal Botanic Gardens, Kew, in 1900, and for about two decades was in charge of the Thalamiflorae and Disciflorae (in the system of Bentham and Hooker). The division of work was, however, not strictly adhered to, and some of Sprague's best taxonomic work concerned the Loranthaceae of tropical and south Africa, for the "Flora of Tropical Africa" and the "Flora Capensis", respectively, and the Bignoniaceae. Later, he was in charge of the American collections. He made, with Mr. (later Dr.) John Hutchinson, a botanical excursion to the Canary Islands in the summer of 1913. He served with the artillery in the First World War and was stationed in India and did some plant collecting in the Punjab. Sprague was awarded the degree of doctor of science by the University of Edinburgh in 1930 and was, the same year, appointed deputy keeper of the Herbarium. He was a fellow of the Linnean Society of London from 1903, and on May 12, 1937, was presented with the Coronation Medal of George VI. He retired from his post at Kew on October 31, 1945.

Soon after his return from military service, Sprague devoted a large proportion of his official and private time to botanical nomenclature and to the study of certain herbals. Those who knew his careful critical researches on the systematics of various groups

tended to regret that he did not concentrate on herbarium taxonomy in the form of monographic work. However, he was mentally and temperamentally well equipped to deal with modern revisions of old herbals and with the intricacies of nomenclature. His accounts of "The Herbal of Otto Brunfels" (*J. Linn. Soc. Bot.*, 48, 79; 1928) and, with E. Nelmes, of "The Herbal of Leonhart Fuchs" (*loc. cit.*, 48, 545; 1931) are models of their kind. For a good many years Sprague was in charge of compilers engaged in preparing the supplements (usually quinquennial) of the "Index Kewensis". There is no doubt that his training of these to the degree of accuracy on which he insisted greatly raised the standard of this important work. It is probable, too, that this supervision of an index to plant names directed his attention to botanical nomenclature in general and to various weaknesses in the International Rules. He attended the International Congress of Plant Sciences, held at Ithaca, New York, in August 1926 and read a paper there under the title "Principles and Problems of Plant Nomenclature". This clearly written paper (published in the Proceedings, 2, 1422; 1929) might be read with advantage by modern nomenclaturists. Sprague became a leader in plans for revision of the rules and largely directed the meetings and debates on this subject at the International Congresses of Cambridge (1930), Amsterdam (1935), and Stockholm (1950). His lucid mind and his undoubted liking for legal form enabled him to enjoy discussions which were sometimes prolonged and sometimes heated.

Sprague was very helpful in training young systematists at Kew, and, though he sometimes flared up rather quickly, he was always kind and painstaking, and anger died quickly and left no malice in him. He was twice married and leaves three children and a widow. After his retirement to Cheltenham he devoted a good deal of time to his hobby of collecting certain special makes of British ceramics and to the Cotteswold Naturalists' Field Club, of which he became president. W. B. Turrill

NEWS and VIEWS

Jodrell Bank Radio Telescope Appeal

An appeal was launched by the University of Manchester at the recent meeting of the Court of Governors for subscriptions to a fund for the radio telescope at Jodrell Bank. The appeal has now been issued over the signatures of Sir Raymond Streat (chairman), Mr. L. P. Scott (deputy chairman), Mr. A. V. Symons (treasurer), Mr. R. B. Barclay (deputy treasurer), and Prof. W. Mansfield Cooper (vice-chancellor). In consequence of the Russian *Sputnik* and the American *Explorer* satellites and lunar probe, all the world knows that the University of Manchester has pioneered in the construction of this 250-ft. steerable radio telescope capable of scientific research on a vast cosmological scale as well as studies of immense practical importance in radio communications and the tracking of satellites used for space exploration. When the building of the instrument was originally proposed, the Council of the University gave enthusiastic support to the ideas of the scientists. Undismayed by the large sums of money involved according to the first estimates—and the difficulties of estimating are obvious—the University embraced the project. The Nuffield Foundation and the Department of Scientific and Industrial Research agreed each to find £200,000. Later it was found essential to revise the first estimates and the Department contributed a further £130,000 on the assumption that the University would find donors willing to cover the balance. It now appears that the University will require at least £150,000 to relieve the telescope from debt and to set scientists free to pursue, without financial anxieties, work of the first order of importance and urgency. If a larger sum were obtainable, further and better work could be done. It is hoped to receive contributions not merely from firms whose products give them a technical and perhaps commercial interest in the work of the Telescope but also from firms, institutions and individuals who would not wish that the result of the University's courage in this matter should be to leave it with unsolved financial problems.

The radio telescope is an immense achievement whether viewed as a stupendous piece of scientific equipment conceived by Prof. A. C. B. Lovell, an unparalleled feat of engineering designed by Mr. H. C. Husband or a fine accomplishment by the many firms engaged on the project, especially the main contractors, the United Steel Companies, Ltd. The increases over the earliest estimates have been accepted as necessary in all the circumstances by both the Department of Scientific and Industrial Research and the University. Indeed, when the University first realized that heavy additional costs were involved, it was nevertheless decided to proceed with the instrument. In reaching this decision, the University relied on the most expert external advice, scientific and technical. As a consequence the instrument was ready to play the part it did in the International Geophysical Year and the developments which have stemmed therefrom. Had the University failed to proceed, Great Britain's contribution to recent world scientific events of great international importance would have been sensibly lessened. The ultimate costs would also have been greatly enhanced. The result of the University's courage is that Britain is first in the field with a telescope of fantastic quality at a cost far below what others will soon be paying for similar instruments. Before opening the appeal, £10,000 was received from Henry Simon, Ltd., and an offer of a further £10,000 from Simon Carves, Ltd. Several small subscriptions have been received from individual donors after Press accounts of the Court meeting. Contributions in the form of seven- or ten-year covenants will be especially welcome. The Bursar of the University will acknowledge donations or supply information to those considering alternative methods of giving support.

The National Research Development Corporation

The Development of Inventions Bill, which received its second reading in the House of Commons on November 14, extends the power of the National Research Development Corporation to make advances by a further ten years from June 1959 onwards, and raises the limit on the amount of advances from £5 million to £10 million. In moving the second reading,

the Parliamentary Secretary to the Board of Trade, Mr. J. Rodgers, explained that unless the former limit was raised, the Corporation would have to abandon many projects already in hand before they could come to fruition and might quite soon find itself unable even to discuss new projects with inventors or research organizations, however important their proposals. Mr. Rodgers also said that it is hoped in future to publish the annual report of the Corporation rather earlier. He referred to the contribution of the Corporation to the establishment of an electronic computer industry in Britain, and also mentioned its sponsoring of the flexible containers for transporting oil developed by research at the University of Cambridge. He said that the Corporation's income had now risen to nearly £200,000. Mr. A. Albu, in welcoming the Bill, mentioned among other new developments a new mechanism for storing energy in the flywheel of a commercial vehicle when braking and making the energy available afterwards for acceleration, and Sir Thomas Merton's diffraction gratings at the National Physical Laboratory, which will have increasing use in spectrometry and metrology. He believes the Corporation should use to the full its power to place development contracts, particularly for new processes or for new machines; that more use should be made of the section of the 1948 Act which enables the Government to ask the Corporation to undertake work which is not economic and for which it would make good a loss if the work was in the public interest; and that the Corporation would further develop its existing good collaboration with the universities and the colleges of technology.

Research and Development in Government Establishments

Answering a question on November 18 in the House of Commons as to the availability of research equipment at the National Chemical Laboratory, Mr. H. Nicholls, Parliamentary Secretary to the Ministry of Works, on behalf of the Lord President of the Council, said that subject to the avoidance of undue interference with its own research programme, the Laboratory is always ready to consider how its resources of equipment and knowledge of special techniques can be utilized by other scientists from industrial laboratories. During the past two years, research workers from seven organizations have spent in all ninety days on experiments with special high-pressure and high-temperature equipment in the Laboratory, and this use is expected to grow. In reply to further questions about scientific and industrial research, Mr. Nicholls said that Government expenditure on scientific research for civil purposes has more than doubled since 1951, and this year the research councils for which the Lord President is responsible will be spending about £20 million, compared with less than £9 million eight years ago. The investigation at the Water Pollution Research Laboratory of the effects of industrial effluents on streams, with the object of developing improved methods of treatment, has been assisted by a contribution from industry through the Federation of British Industries which next year will amount to £13,000. The Pest Infestation Laboratory has developed a rapid and reliable instrument, now available commercially at a cost of about £50, for determining the moisture content of cereals stored in bulk, and the National Institute of Agricultural Engineering of the Agricultural Research Council has examined the range of moisture meters available for testing the moisture content of grain stored on the farm. The Road Research Laboratory is investigating means of electrically heating road surfaces to mitigate dangers from frost, and it is hoped shortly to lay another experimental surface of this type on a new road-bridge to be constructed at Slough. The work of the Laboratory on the design and siting of snow fences has been outstandingly successful and offers large savings of cost and labour if the snow fences are correctly sited. The British Coal Utilization Research Association has shown that with proper mechanical firing equipment the efficiency of use of small coal in shell-type boilers can be high. Further research and development on automatic handling and control are in progress, in association with the National Coal Board, which is also developing work on the manufacture of briquettes from small coal.

Science and Mathematics in Schools

In answer to a question asked in the House of Commons on November 18, the Joint Under-Secretary of State for Scotland, Mr. N. Macpherson, said that according to estimates by the education authorities and managers of grant-aided schools, 97 teachers with first- or second-class honours degrees were required in October 1957 to teach science and 119 to teach mathematics. A further 152 graduate teachers were needed to teach these subjects in the junior classes of secondary schools. Representations for the release from National Service of third-class honours graduates in science and mathematics to enable them to return to the schools are under consideration.

Broadcasting, Television and the Schools

In an address to the School Broadcasting Council on November 7, Sir Ian Jacob, director-general of the British Broadcasting Corporation, referred particularly to the dependence of Great Britain, and possibly its survival, upon the widest possible diffusion of scientific skills and knowledge. He suggested that the British Broadcasting Corporation might be able to make, in its own way, "a new and massive contribution to the understanding of science in the secondary modern schools, where the need perhaps is greatest and where the shortage of good teachers is likely to be most acute". Sir Ian said he had recently received a deputation comprising the Presidents of the Royal Society and the British Association and the Chairman of the Advisory Council on Scientific Policy, who had come to urge that the Corporation should do its best to interest the broad mass of the people in scientific development and to present science as vital to the well-being of our contemporary world. The B.B.C., he said, is already doing this job, and it proposes to put all the resources it can behind it. The task must begin in the schools, and Sir Ian thought that television might be opening up wholly new possibilities in school broadcasting.

Extensions to the Duncan Flockhart Research Laboratories, Edinburgh

Extensions to the Duncan Flockhart Research Laboratories in Edinburgh, which were opened on November 14 by Prof. John Bruce, president of the Royal College of Surgeons of Edinburgh, consist of additional development and biological laboratories. The former are in the chemical laboratory building,

which also houses the analytical control department and the library. The new biological laboratories form part of a quadrangle of buildings in which biological research and assay are carried out. The extensions were designed by members of the staff, the principal contractor of laboratory furnishing being Nathaniel Grieve. Lord Ferrier, chairman of the T. and H. Smith Group of companies, of which Duncan Flockhart became a member in 1952, presided at the opening ceremony, and an address of thanks to Prof. Bruce was delivered by Dr. F. R. Smith, director of Duncan Flockhart and Co., Ltd., who is in charge of the Group's research and development activities.

The research staff includes chemists, biologists, pharmacists and a medical unit headed by a physician. The chemists are concerned with new compounds with biological activity which may become new drugs for use as analgesics, local anæsthetics, muscle relaxants and for the treatment of diseases involving nervous and muscular defects. They work in close association with the biologists responsible for testing the new compounds for their potency, absence of side-effects, etc. The pharmacists work on the presentation of drugs to ensure maximum effect and convenience for doctor and patient and on problems of stability and analysis. The medical unit makes arrangements for the clinical trials of new drugs. An extensive library is maintained which acts as an information centre for the research staff and the other technical staff of the Company.

National Science Foundation Co-operative Graduate Fellowships

The National Science Foundation has announced a new programme of co-operative graduate fellowships under which approximately 1,000 fellowships will be offered to graduate students in the sciences and engineering. To be eligible, candidates must be citizens of the United States and have special aptitude for advanced training and productive scholarship in the sciences. This programme is in addition to the Foundation's regular predoctoral, postdoctoral, senior postdoctoral and science faculty fellowship programmes. In the first experimental year of operation, applicants may apply to study at one of 115 designated colleges and universities. Applications will be forwarded—together with the institution's recommendations—to the National Science Foundation, where they will be considered by panels of scientists appointed by the National Academy of Sciences—National Research Council. Fellows will receive a basic annual stipend of 2,200 dollars with the option of nine or twelve months tenure. Supplemental support may be extended by the institutions themselves to encourage Fellows to undertake limited teaching responsibilities during tenure of their fellowships. In addition, the Foundation will provide each institution, in lieu of tuition fees, with a fixed amount for each co-operative graduate Fellow at that institution. Co-operative graduate fellowships will be offered in the mathematical, physical, medical, biological and engineering sciences, as well as in anthropology, psychology (excluding clinical psychology), and in certain social sciences, including geography, mathematical economics, econometrics, demography, information and communication theory, experimental and quantitative sociology, and the history and philosophy of science.

National Museum of Canada

The report of the National Museum of Canada for 1955–56 (pp. iii+140 (17 plates). Ottawa: Queen's Printer, 1957. 1.50 dollars) is far more than a formal report on the work of the institution, for it also includes papers on research work undertaken by or in collaboration with the staff. The record of the general activities includes an impressive amount of educational work carried out through the media of exhibits, lectures, publications, photographs, film strips and correspondence. Visits to the Museum by organized groups were also encouraged, and some 4,000 individuals attended the Museum in this way. Each group was provided with a guide. The papers published in this report include such diverse subjects as archæological work on Southampton and Walrus Islands, Tertiary mollusca from Princeton, British Columbia, Paleocene mammal teeth from Alberta and a bibliography of Canadian anthropology for 1955.

Equipment for Archæology and Geology

Messrs. P. J. Dutt and Co., Ltd., of Alfred Place, Store Street, London, W.C.1, have recently issued a comprehensive and fully illustrated catalogue entitled "Equipment for Archæology and Geology", in which the emphasis is perhaps on geology rather than archæology, though the requirements of archæologists are by means neglected, being often coincident with those of geologists. All branches of geology are catered for, including both field and laboratory work, mineralogy, petrology and palæontology. The soil scientist, too, will find some of the items listed of interest. The instruments and equipment are grouped under the following headings: collecting; mapping and surveying; specimen preparation, display and preservation; laboratory equipment, including microscopes; and teaching aids. The catalogue covers a wide variety of field and laboratory activities, and should prove useful to both amateur and professional geologists, archæologists and museum curators. Messrs. Dutt also point out they are agents for Ward's Natural Science Establishment, New York, and Soiltest Incorporated, Chicago, from whom they are prepared to import specialities not available in the United Kingdom.

Rheology Abstracts

Very soon after the British Rheologists' Club was started in 1940, its first *Bulletin* appeared, "gratis, to members of the Club only". This contained notices of meetings, news of interest to members and abstracts of recent rheological papers. After the publication of the fifty-third *Bulletin* (December 1957) the sponsors, now called the British Society of Rheology, decided to change the form of publication, the *Abstracts* being issued separately from the *Bulletin*. The latter contains news for members, summaries of papers given at conferences, etc., while the former is now headed "A Survey of World Literature" (1, No. 1; May 1958. Pp. 31. Four issues a year: subscription £2 per volume of four issues. London: Pergamon Press, 1958. Published for the British Society of Rheology).

The organization of such a venture by honorary abstractors alone is no small undertaking. The coverage must depend on chance factors involving the interests of the volunteers. The Society has decided to start with the material available and to

expand coverage as opportunities arise. Already, more than a hundred journals are abstracted regularly. The aim is to direct attention to papers in journals which are fairly easily obtained and understood, while giving rather fuller abstracts of worthwhile articles in obscure journals or less-known languages. The classification is under seven headings: theoretical; instruments and techniques; metals and other solids; polymers, elastomers and viscoelastic materials; pastes and suspensions; liquids; general (miscellaneous). It is a pity that attempts made some ten years ago to start an international rheology abstract journal proved abortive. To-day, several of the national societies provide excellent abstract services, a situation which results in much overlapping. Nevertheless, in existing circumstances, the British Society of Rheology had no alternative but to organize its own survey and, until an international service can be organized, the *Abstracts* in their new form should prove very valuable to rheologists both in Britain and abroad.

History of Thermometry

A VERY interesting booklet has been issued by Messrs. Negretti and Zambra entitled "A Story of Temperature Measurement" (pp. 20. London, 1958), in which the history of the thermoscope and the liquid-in-glass thermometer is outlined from the earliest times up to the most modern forms. The earliest forms of thermoscope were devised for medical purposes, and arbitrary 'degrees' of heat and cold (which were both regarded as positive qualities) were called upon to indicate a patient's condition. Measurement began early in the seventeenth century, but it is uncertain to which of three or four inventors the credit for the construction of the first thermometer is to be ascribed. In the earliest instruments, variations in the volume of air enclosed in a bulb were used to indicate changes in temperature, but ignorance concerning the effect of atmospheric pressure vitiated their use for precise scientific purposes. The present-day forms of liquid-in-glass thermometer—the Fahrenheit, Réaumur and Celsius—appeared almost simultaneously early in the eighteenth century, and the circumstances of their invention, which have been widely misrepresented, are accurately described. The account is enriched by a large number of illustrations, many of which show instruments to be seen at the Science Museum, South Kensington, and by a useful bibliography. It can be recommended as a readable and trustworthy summary of an interesting chapter in the history of science.

Royal Australian Chemical Institute: Officers

MR. L. W. WEICKHARDT, technical director of Imperial Chemical Industries, Australia and New Zealand, Ltd., has been elected president of the Royal Australian Chemical Institute for 1958–59, and Mr. W. H. Wainwright has been elected vice-president. The other members of the Council are Mr. W. S. McGowan and Mr. C. I. Cox (New South Wales); Dr. J. M. Harvey and Dr. H. E. Dadswell (Queensland); Mr. R. G. Cooke (South Australia); Mr. J. L. Flounders and Dr. J. A. Allen (Tasmania); Dr. D. R. Zeidler and Dr. A. L. G. Rees (Victoria); Dr. D. E. White and Mr. L. R. Allison (Western Australia); Dr. A. Walkley (honorary general secretary); and Mr. G. Junck (honorary general treasurer).

University News: Birmingham

THE title of reader in physics has been conferred on Dr. J. H. Fremlin, senior lecturer in physics, and that of reader in comparative neurology on Dr. J. T. Eayrs, senior lecturer in neuro-anatomy and at present Henry Head Research Fellow of the Royal Society in the Department of Anatomy. Approval has been given for the establishment of a chair of organic chemistry within the Department of Chemistry. The following appointments have been made: Dr. G. V. Chester, to be lecturer in mathematical physics; Dr. M. H. Cardew and Dr. M. B. King, to be lecturers in chemical engineering.

Bristol

THE following appointments have been made: Miss Dorothy J. Cooper, to be lecturer in education; and Dr. A. J. Forty, to be lecturer in physics.

The following gifts, among others, have been received by the University: a legacy from Mrs. Hilda Grace Pickard of her residuary estate (subject to three life interests) upon trust to create an endowment fund and to apply the income for the purpose of research into the alleviation of cancer, to be named the Pembery Research Trust—funds totalling £10,084 representing approximately two-fifths of the total residuary estate have now been transferred to the University; £6,300 from the Department of Scientific and Industrial Research to the Department of Physics towards the cost of Prof. C. F. Powell's research on heavy mesons and hyperons by the photographic method; grants totalling £6,086 from the Department of Scientific and Industrial Research to the Department of Physics for salaries and equipment for research work under Prof. Powell; £1,100 from the National Coal Board to the Department of Physical and Inorganic Chemistry for a continuation of the study of reactivity of carbon surfaces with oxygen; and £1,700 from the Department of Scientific and Industrial Research for research assistants and equipment; £1,315 from the Ministry of Supply to the Department of Aeronautical Engineering for research on the prevention of flutter by damping; £1,000 from the Agricultural Research Council to the Department of Veterinary Medicine for research on the nutrition of the baby pig; and £1,000 from the Nuffield Foundation to the Department of Veterinary Anatomy for research on age changes in the vertebral disk of the cat.

London

SIR JOHN ATKINS has been admitted as the first Fellow of Queen Elizabeth College in recognition of his unique service. It is to his vision and determination that the College owes its existence, and he has worked for it continuously since 1911 when, as honorary secretary of the Appeal Committee, he inspired a few generous benefactors to subscribe the funds needed for the erection of the present buildings. He remains a member of the Governing Body, to which he was elected in 1912 and of which he has been chairman since 1922. He is being succeeded as chairman by Sir George Allen, secretary of the British Association.

In the paragraph on 'Commonwealth Fellowships' in *Nature* of November 8, p. 1276, the percentage of overseas students at the Imperial College of Science and Technology, London, was quoted as 38, a figure which has been reported previously in the Press. The Registrar of the College states that this refers

only to postgraduate students (full-time and part-time). The percentage of undergraduate students from overseas is only 10 per cent. The total number of full-time overseas students has been rising steadily since the programme of expansion started in 1953, but the proportion has scarcely changed. In 1952–53 there were 312 from overseas out of a total of 1,653 full-time students, or 19 per cent. Last session the corresponding figures were 528 out of 2,437, or 22 per cent. The number this term is 552 out of 2,580, or 21 per cent.

The Night Sky in December

New moon occurs on Dec. 10d. 17h. 23m. U.T., and full moon on Dec. 26d. 03h. 54m. The following conjunctions with the Moon take place: Dec. 22d. 05h., Mars 4° N. Mercury rises about two hours before the Sun at the end of the month, but conditions are not favourable for observation. Venus is too close to the Sun for observation. Mars sets at 6h. 05m., 4h. 55m. and 4h. 00m. at the beginning, middle and end of the month, respectively. Mars retrogrades until December 20, after which date it resumes its eastward motion among the stars; it is in Aries throughout December. Its stellar magnitude decreases during the month from $-1{\cdot}6$ to $-0{\cdot}6$, its distance from the Earth increasing from 49 to 67 million miles. Jupiter rises at 5h. 50m., 5h. 10m. and 4h. 25m. on December 1, 15 and 31, respectively; it is east of α Libræ. The stellar magnitude of Jupiter is $-1{\cdot}3$; conditions for observation are not very favourable. Saturn is too close to the Sun for observation. Occultations of stars brighter than magnitude 6 are as follows, observations being made at Greenwich: Dec. 23d. 22h. 33·6m., 8 Tau. (*D*); Dec. 23d. 23h. 03·2m., 64 Tau. (*D*); Dec. 28d. 20h. 29·2m., A^1 Cnc. (*R*); Dec. 29d. 04h. 04·0m., α Cnc. (*D*); Dec. 29d. 04h. 59·8m., α Cnc. (*R*). *D* and *R* refer to disappearance and reappearance, respectively. The Geminid meteors are active during December 9–14, conditions being very favourable; the radiant is near R.A. 7h. 28m., Dec. + 32°. The Ursid meteors are active on December 21, but conditions for observation are unfavourable. The winter solstice occurs on Dec. 22d. 09h.

Announcements

On November 22, H.M. the Queen conferred the Order of Merit on Viscount Samuel. This award is a tribute to a life-time of devoted public service, including fifty years as a Privy Councillor.

Dr. Vittorino Veronese, a lawyer and formerly president of Catholic Action in Italy, has been elected director-general of the United Nations Educational, Scientific and Cultural Organization for a period of six years.

The managing trustees of the Drummond Trust will consider, in March 1959, applications for a Drummond Fellowship for research in nutrition. It may be a Senior or Junior Fellowship, depending on the qualifications of the person selected. The value of a Senior Fellowship would be £1,100 per annum with expenses grant and superannuation, and of a Junior Fellowship £500 per annum with expenses grant. The Fellowship will normally be tenable for two years. Full particulars can be obtained from the Honorary Secretary, Drummond Trust, University College London, Gower Street, W.C.1. Completed application forms must be received not later than January 31, 1959.

The Royal Agricultural Society of England offers annually a medal together with an award of one hundred guineas for research work of outstanding merit carried out in the United Kingdom which has proved, or is likely to prove, of benefit to agriculture. Recommendations for this award can be made by the heads of university departments, research stations and institutes. No direct application by candidates will be considered. Recommendations for the next award must be submitted to the Secretary, Royal Agricultural Society of England, 35 Belgrave Square, London, S.W.1, not later than January 31, 1959, accompanied by nine copies of a brief statement of the candidate's attainments and a list of his publications.

The fourth Biennial Conference on Carbon, on "The Physics and Chemistry of Carbon Surfaces", will be held at the University of Buffalo during June 15–19, 1959. Information can be obtained from Carbon Conference, University of Buffalo, Buffalo 14, New York.

A meeting of the Parasitology Group, Institute of Biology, will be held in Edinburgh during March 19–23, 1959. The closing date for registration is February 28. Further particulars of the meeting can be obtained from Miss J. Mahon, Department of Zoology, Bedford College, Regent's Park, London, N.W.1.

The Institution of Electrical Engineers is holding a Convention on Thermo-Nuclear Processes, during April 29–30, 1959. The probable range of topics is as follows: basic physics of thermonuclear processes; prototype British thermonuclear experiments; constructional features of ZETA 1; design problems of future ZETA-type systems; possibilities of direct conversion from nuclear to electrical energy. Further information can be obtained from the Secretary, Institution of Electrical Engineers, Savoy Place, London, W.C.2.

The next meeting of the Plant Phenolics Group will be held on January 6, 1959, at the Queen Elizabeth College, London, W.8, under the chairmanship of Prof. R. D. Haworth. The subject will be "Chemistry of Condensed Tannins". Speakers will include Drs. B. Brown, D. E. Hathway, W. E. Hillis, E. A. H. Roberts, D. Roux and T. Swain. Further information can be obtained from the honorary secretary, Dr. T. Swain, Low Temperature Research Station, Downing Street, Cambridge.

Under the provisions of the Fulbright Programme, travel grants are available to citizens of the United Kingdom and dependent territories to go to the United States for an academic or educational purpose, provided that they have financial support in dollars for the visit, and have been accepted by an American institution of higher learning. Grants cover the cost of direct travel between a candidate's home and the American university or institution, and are available during June 1, 1959—April 1, 1960. Applications must be submitted by March 14, 1959 (for those travelling between June 1, 1959, and August 15, 1959) or by June 1, 1959 (for those travelling between August 16, 1959, and April 1, 1960). Application forms and further information can be obtained from the United States Educational Commission in the United Kingdom, 71 South Audley Street, London, W.1.

INTERNATIONAL ATOMIC ENERGY AGENCY

THE first annual report of the Board of Governors of the International Atomic Energy Agency to the General Conference* covers the period October 23, 1957–June 30, 1958, in which the membership of the Agency rose from twenty-six to sixty-six. Much of the work of creating the technical and administrative services needed both to implement the initial programme, which allots high priority to activities that will give the maximum benefit from the peaceful application of nuclear energy in improving the conditions and raising the standard of living of people in the under-developed areas, and to co-ordinate the Agency's activities with those of the United Nations and the Specialized Agencies, has been completed and operations commenced in some of the fields assigned by its statute. Excluding posts in the Division of Language Services, some two-thirds of the established posts in the Agency are in the scientific and technical divisions, and in the 111 professional staff appointed by June 30, 1958, twenty-eight nationalities were represented. Deputy directors-general were appointed in December for each of the three technical departments: training and information; technical operations; and research and isotopes. Experience so far has confirmed the Preparatory Commission's expectations that initial activities in regard to the supply of materials, reactors and safeguards would consist largely of planning, collecting and exchanging information, surveys and technical advice.

The major technical assistance activity already operating is the Agency's international training programme, which embraces the training of specialists in all important peaceful applications of nuclear energy by the award of training fellowships and exchanges of scientists and experts. For these fellowships a fund of 250,000 dollars was established, and in addition 268 subsidized or fully paid fellowships for training and research in institutions in their own countries were offered by member States. A field study is being made in Latin American countries to determine their requirements for training in the peaceful uses of nuclear energy and the availability of existing facilities. It is expected that the basic technical library will be functioning by the end of 1958, and the Agency's scientific and technical documentation service is already providing abstracts of scientific material and specialized bibliographies. It is also proposed to issue lists of all conferences in this field held throughout the world and to assist member States and scientific and technical organizations in planning and timing such meetings.

A provisional manual on radiation protection is planned, and an expert panel has been convened, while the collection and evaluation of data on the disposal of radioactive waste have commenced. The reactor programme will be divided into the physics and chemistry of reactors; problems of engineering; and production of nuclear energy. Data are being collected for an international reactor directory covering all types of power, research and training reactors. Under isotopes and research, plans are being made for forming composite isotope teams, including experts on applications of radioisotopes and radiation, to be sent on request to countries in the less-developed areas, and a survey is being made with a view of compiling an international catalogue of radioisotopes. The work of the Agency is further displayed in its Programme and Budget for 1959*, in which an analysis of its proposed expenditure of 6·725 million dollars (including 550,000 dollars on scientific information and conferences, 2·575 million dollars on technical assistance and 1·050000 million dollars on regulatory activities) is accompanied by a description of the functions and programme of each of its departments.

* First Annual Report of the Board of Governors of the International Atomic Energy Agency to the General Conference covering the period from 23 October 1957 to 30 June 1958. Pp. ii+53. (Vienna: International Atomic Energy Agency, 1958.)

* International Atomic Energy Agency. Programme and Budget for 1959. Pp. vii+94. (Vienna: International Atomic Energy Agency, 1958.)

NETHERLANDS–NORWEGIAN JOINT ESTABLISHMENT FOR NUCLEAR ENERGY RESEARCH

THE sixth annual report* of the Netherlands–Norwegian Joint Establishment for Nuclear Energy Research (J.E.N.E.R.), the joint research and training centre sponsored by the Dutch Reactor Centrum Nederland (R.C.N.) and the Norwegian Institut for Atomenergi (I.F.A.), which has now been published, describes the work of the Establishment during the period July 1, 1956–June 30, 1957. The governing board consists of a joint commission comprising three Dutch and three Norwegian members, and the work of the Establishment is directed by Mr. Gunnar Randars, who was appointed by the Institut for Atomenergi with the approval of the Reactor Centrum Nederland. The staff is grouped into six divisions—physics, engineering, civil engineering, chemistry, isotopes, and health physics—in addition to the administration, and during the period under review totalled 180, of which fifty-four are classified as scientists and engineers and sixty-four as technicians and skilled workers.

The research reactor, JEEP, which is fuelled with natural uranium and moderated and cooled by heavy water and which is situated at Kjeller, was in almost continuous operation at 450 kW. during the year, and approximately 92 MW. days of energy were released. Complete shut-downs occurred only for holidays and for the semi-annual inspection work. The Halden boiling-water reactor (HBWR) which uses heavy water, and which was designed by the Establishment, is being built by the Institut for Atomenergi and is now at an advanced stage of construction; it was expected to go critical some time during 1958. The civil engineering work has been completed; the

* Sixth Annual Report, July 1956–June 1957, of the Netherlands–Norwegian Joint Establishment for Nuclear Energy Research. Pp. 31. (Kjeller, near Lillestrøm: JENER, 1958.)

workshop in the control building has been equipped; and the offices on the first floor of the building are in use. Most of the mechanical components of the reactor are being made by Norwegian firms, but the uranium fuel will be supplied by the United Kingdom Atomic Energy Authority and the heavy water by the United States Atomic Energy Commission. The reactor will be operated at low temperatures to begin with, and preliminary investigations have shown that 2*S*-aluminium withstands these low temperatures well and therefore is suitable as canning material for the initial fuel charge.

Information concerning the probable kinetics of the reactor has been obtained through void-coefficient experiments conducted by the physics division and by the use of a reactor simulator which was built specially for this purpose. The simulator consists of an analogue computer, loaned by the Norwegian Defence Research Establishment, to which has been added various units for the simulation of reactor kinetics and xenon poisoning and a multiplier circuit.

The nuclear ship-propulsion group has concentrated its attention on the use of uranium oxide – light water lattices for ship reactors. Parametric analyses of various fuel-moderator systems have been carried out, and optimization studies of reactor plant components have been made. Problems relating to both normal as well as adverse operational conditions, such as collisions at sea, groundings, fire and explosion hazards, have been considered and discussed with the appropriate Norwegian maritime authorities.

In addition to the void-coefficient experiments the physics division has continued its exponential experiments on heavy water – natural uranium lattices which it is carrying out in co-operation with A. B. Atomenergi at Stockholm. A report of measurements on clean lattices has been published (*J. Nuclear Engineering*, 3; 1956) and a report on cluster type rods has been issued by A. B. Atomenergi (AEF–65). A Nonius general-purpose camera has been added to the X-ray equipment and X-ray work has been mainly concentrated on phosphoric acid. The investigation of capture gamma circular polarization has continued and work on the gamma-spectrum of fission has been started. The health physics service of the Establishment was intensified during the period under review and the report mentions that only one member of the staff received a dose in excess of 5r. and that 81 per cent received less than 1r. The service controls about 150 persons.

Details are also given in the annual report of the production and shipments of radioisotopes; of the activities of the chemistry and metallurgical sections of the Establishment; of the reports and publications published by the Establishment and members of the staff; of the Establishment's reactor courses and of the new reactor school being opened in 1958 with a nine-week full-time postgraduate course in fundamentals of nuclear engineering; and of the personnel and accounts of the Establishment.

RESEARCH AND DEVELOPMENT IN THE B.B.C.

APART from the maintenance and steady improvement of a nation-wide sound and television service, the manner in which the Engineering Division of the B.B.C., and particularly of its Research and Designs Departments, continues to make technical progress, is well illustrated by the B.B.C. Engineering Division Monographs, of which Nos. 15–19 have been published during the past few months* (reference was made to Nos. 12–14 in *Nature*, 181, 1046; 1958). These deal with a variety of subjects, from the quantitative measuring technique which is a necessary tool in the transmission and reproduction of high-quality sound to an appraisal of the results of the experiments made by the B.B.C. in colour television.

Monograph No. 15, entitled "New Equipment and Methods for the Evaluation of the Performance of Lenses for Television", outlines the photo-electric method of testing lenses and describes a new optical bench developed for the purpose. The factors affecting the quality of a television picture are discussed, and formulæ are developed on an experimental basis for an index of quality for both monochrome and colour television.

The analysis and measurement of the extremes of sound programme-levels are dealt with in Monograph No. 16 in two parts: (1) "Investigation of Extreme Values of Sound Pressure", by D. E. L. Shorter and W. I. Manson; and (2) "A Description of an Optical Instrument for Monitoring Sound Signals", by E. R. Wigan. An optical projection type of instrument has been developed, the range of indication of which is sufficient to deal with the most difficult programme material. While the instrument has a limited field of application to sound broadcasting, it has obvious advantages for the control of sound channels in television.

"The Design of a Linear Phase-Shift Low-Pass Filter", by L. E. Weaver (Monograph No. 17), describes the theoretical and practical details of the design of a very linear phase-shift low-pass filter intended to remove noise and other irrelevant information above approximately 3 Mc./s. from the output of a television camera control unit. A "Note on Random Fluctuation Noise in Image Orthicon Camera Tubes", by R. D. A. Maurice, is appended and revises some of the conclusions in an earlier monograph on the distribution of noise over the grey scale of a picture.

Monograph No. 18 forms an interesting highlight in the series under review and is entitled "The B.B.C. Colour Television Tests: an Appraisal of Results", by W. N. Sproson, S. N. Watson and M. Campbell. This describes the results of field trials conducted during 1955–57 in viewers' homes by the Research and Designs Departments of the Corporation after preliminary experiments and the development of suitable receivers in the laboratory. Since the tests were completed, a further series was carried out during 1957–58 and the results are now being analysed.

* B.B.C. Engineering Monographs. No. 15: New Equipment and Methods for the Evaluation of the Performances of Lenses for Television. By W. N. Sproson. Pp. 16. No. 16: Analysis and Measurement of Programme Levels. Part 1: Investigation of Extreme Values of Sound Pressure. By D. E. L. Shorter and W. I. Manson. Part 2: A Description of an Optical Instrument for Monitoring Sound Signals. By E. R. Wigan. Pp. 31. No. 17: The Design of a Linear Phase-Shift Low-Pass Filter. By L. E. Weaver. Pp. 23. No. 18: The B.B.C. Colour Television Tests—an Appraisal of Results. By W. N. Sproson, S. N. Watson and M. Campbell. Pp. 39. No. 19: A V.H.F. Television Link for Outside Broadcasts. By K. C. Quinton. Pp. 20. (London: British Broadcasting Corporation, 1957 and 1958.) 5s. each.

The field trials on which the B.B.C. now reports extended over a total period of seventeen months and involved the analysis of more than a thousand questionnaires, filled in by members of the B.B.C. staff and others who watched the results on special sets. So far as reception of the colour picture is concerned, the B.B.C.'s verdict is that the colour pictures produced by the N.T.S.C. system as adapted to 405 lines, with the picture sources and display tubes that are at present available, are satisfactory. The problem of registration with the three-tube colour camera requires attention, and certain features of the display tube could with advantage be improved, but the technical performance of the system is adequate for a satisfactory colour television service in the frequency bands at present in use. The tests radiated from Crystal Palace during November 1956–April 1957 included live studio performances, film and slides. Of the observers, 89 per cent regarded the reception of the live scenes as satisfactory. The 35-mm. film was regarded as satisfactory by 100 per cent of the observers, the 16-mm. film by 93 per cent, and the slides by 98 per cent. The compatibility of the transmissions was very good indeed. This means that the quality of ordinary black and white television, when received on a colour television set, was found to be generally satisfactory; and likewise the quality of the colour transmissions, when received in black and white on ordinary television sets, was completely acceptable to 94 per cent of technical observers.

The results of the tests have been communicated to the Television Advisory Committee, which has the task of advising the Postmaster-General on the whole field of television. The results have also been sent to the International Radio Consultative Committee which recently met in Moscow to consider colour television. The B.B.C. will carry out further experimental transmissions from time to time. It is pointed out that there are many other problems to be solved: for example, the production of a reasonably priced colour-receiving set and agreement on the future standards to be applied to the development of television in the United Kingdom. The decision whether or not there is to be a public service of colour television, and if so the system to be used, rests with the Postmaster-General.

A national television network requires to be adequately supported by inter-connecting line and radio links capable of transmitting without distortion the complex signals conveying the sound and vision information. Where outside broadcasts are concerned, mobile equipment is usually necessary, and the design and development of such equipment is described in Monograph No. 19, by K. C. Quinton, under the title "A V.H.F. Television Link for Outside Broadcasts". This provides, first, a brief historical introduction to the problems of radio linkage, leading to the need for using ultra-high frequencies, with particular reference to moving-camera applications and to propagation over water. The relative merits of amplitude and frequency modulation are explored in theory and practice; and details are given of the equipment developed for use in the frequency-range 610–660 Mc./s. The first year's operational experience with such equipment has been very successful.

ROAD RESEARCH

THE work of the Road Research Laboratory is concerned partly with the behaviour of traffic on the road, and partly with the performance of materials and with the methods of construction of the road itself. The Laboratory's annual report for 1957* is interesting and well presented.

Some problems of traffic and safety can be solved by a controlled experiment. For example, the Laboratory conducted a full-scale experiment with streams of traffic weaving through each other as the vehicles entered and left a roundabout. This led to an empirical formula, from which the limiting traffic flow could be predicted accurately. The Laboratory has also developed an apparatus for measuring accurately the resistance of a road surface to skidding; one graph shows a seasonal variation of this resistance which corresponds closely with the seasonal variations in the number of skidding accidents.

To study other problems, the Laboratory conducts various field surveys. For example, a survey of the flow of traffic in the streets of London and Glasgow showed an average journey-speed of ten miles per hour with vehicles stopped for about a third of their journey time. Detailed field studies of accidents suggest that the doors of British cars tend to jam in a crash, while the doors of American cars tend to fly open. Their conclusion from a study of reports of a sample of fatal accidents was that 13 or 14 per cent of fatal accidents involved a person who had drunk alcohol (the official statistics suggest a figure of only 2 per cent), and showed further that, "one half of the drivers and more than one half of the pedestrians involved in fatal accidents at night had been drinking".

Experiments to reduce accidents have sometimes been very successful: a big roundabout can eliminate three-quarters, and a smaller roundabout a half, of the accidents at an intersection. Sometimes success is more elusive. A full-scale attempt to reduce road casualties in Slough over a two-year period produced only an "apparent reduction" compared with the increasing numbers of casualties in Great Britain as a whole, which must have been something of a disappointment. Perhaps it was a mistake for the Laboratory to be too much concerned with traffic conditions in a town so close at hand.

In the work on materials and methods of construction a major experimental section of road has been constructed as part of the new north-bound carriageway of the Great North Road at Alconbury Hill in Huntingdonshire: there are seventy different variations in the pavement construction within a length of 2¼ miles, although the passing motorist is probably only aware of the changes at one or two points in this length. This experiment is concerned with fairly conventional pavement construction, but it is interesting to read of the continued satisfactory performance of some other experiments of previous years when lengths of cement-stabilized gravel base

* Department of Scientific and Industrial Research. Road Research 1957: The Report of the Road Research Board with the Report of the Director of Road Research. Pp. iv+93+8 plates. (London: H.M. Stationery Office, 1958.) 5s. 6d. net.

were constructed. Such a base is inherently cheaper and quicker to construct than a normal base; perhaps British engineers in the past have concentrated too much on the stabilization of the soil that happens to be on the site, and have given insufficient attention to the possibility of stabilizing low-grade unwashed gravel which may be available close by. Work on concrete and bituminous materials is also described.

The report begins with an attempt to gauge the importance of the road problem in Britain. The cost of road accidents is about £100 million a year, and that of time and fuel wasted in congested traffic is several times that figure. The present programme of road improvements is based on information that appears to be inadequate as a basis for design, and in comparison with the sums of money that have been mentioned above the expenditure on road research is negligible. The civil engineering industry itself does relatively little research, and the paucity of the support which the work of the Road Research Laboratory receives can be gauged from a disturbing sentence on the Alconbury Hill experimental section which ". . . was planned some twelve years ago" but was only constructed last year. This is a straightforward experiment for which a site should have been found so that the work could be carried out well in advance of the present road-construction programme. It must be hard to continue with research that apparently receives slight encouragement, and know that for lack of design data the new roads that are now being built are probably not so good as they could be.

A. N. Schofield

JANE COFFIN CHILDS MEMORIAL FUND FOR MEDICAL RESEARCH

THE Jane Coffin Childs Memorial Fund for Medical Research, of New Haven, Connecticut, made appropriations totalling 312,779·93 dollars in support of research and fellowships in cancer for the year July 1, 1957–June 30, 1958. This brought to slightly more than four million dollars the total distributed by the Fund since its establishment in 1937.

Support is given by the Fund to research in both the basic and clinical sciences; for postdoctoral fellowships providing opportunity for advanced training and research; and for conferences and meetings of national and international societies concerned with cancer research. Among publications to the support of which the Fund has contributed since it helped to establish them are the journal, *Cancer Research*, and the "Atlas of Tumor Pathology".

Applications for research grants and fellowships are reviewed by the Board of Scientific Advisers, directed by Dr. M. C. Winternitz, three times a year at the offices of the Jane Coffin Childs Memorial Fund for Medical Research, 333 Cedar Street, New Haven 11, Connecticut.

Although most of the Fund's grants are given to American investigators, no geographical restrictions are placed on its allocations. Austria, Britain, France, Japan and Sweden are represented on the current list of grants for 1958. Dr. Bengt E. G. V. Sylvén, associate professor of experimental cancer research in the Karolinska Institute at Stockholm, received a first grant (30,000 dollars for three years) for development of cytochemical methods to be used in attacking a long-standing controversial question in cancer—the relation of proteolytic enzymes in the malignant cell to the penetration of surrounding tissues by cancer. Dr. Jacques Monod, director of the Department of Cellular Biochemistry at the Pasteur Institute, Paris, received a fifth grant (totalling 29,400 dollars since 1954) for studies of specific enzymes involved in the selective penetration of certain organic molecules into bacterial cells. Grants made to the Institute of Cancer Research, Royal Cancer Hospital, London, beginning in 1938 when the late Sir Ernest Kennaway, then director of the Institute, visited the Fund in New Haven, now total 73,500 dollars. American investigators supported by the Fund in 1958 were working chiefly in university and medical school departments of the basic and clinical sciences, ranging from genetics and botany to surgery and medicine.

Among the long-term programmes at present supported by the five-year grants is that of Dr. Charles B. Huggins and his associates (25,000 dollars a year) at the Ben May Laboratory of Cancer Research, University of Chicago.

In accordance with the developing trend in most of the research on cancer, biochemical approaches outnumber all others in the work of both investigators and Fellows supported by the Fund, with especial concern for the chemical reactions in normal and neoplastic cells and tissues and with particular interest in protein and nucleoprotein metabolism. These and other chemical approaches to the problems of cancer were being studied in tumour and other viruses, in immunological mechanisms, in connexion with the steroid hormones.

Among other grants made by the Fund for the first time in 1958 are those to Dr. L. L. Engel (Massachusetts General Hospital) for work on methods for studying urinary steroid metabolites in cancer; to Dr. E. H. Stotz (University of Rochester) to investigate the occurrence and role of peroxidase in proliferating tissue and its response to hormones; to Drs. R. W. McKee and H. Cook (University of California) for work on physico-chemical and biological characterization of nucleic acids and proteins from several different ascites tumours; to Prof. J. N. Davidson (University of Glasgow) to investigate nucleic acid metabolism in cancer tissue; to Dr. Osamu Hayaishi (Kyoto University) for work on the biological synthesis and degradation of peptides and proteins; and to Dr. Stanfield Rogers (University of Tennessee) to investigate the mechanism of action of the Shope papilloma virus in producing papillomas in rabbit epithelium.

New Fellows supported by the Fund in 1958 include Dr. P. Ottolenghi (Copenhagen), Dr. G. L. Hagen (Harvard), Dr. M. Richter (Indiana), Dr. L. Del Gatto (California), Dr. E. V. W. Yamada (U.S. National Institute of Arthritis and Metabolic Diseases), Dr. K. R. Hanson (New York), Dr. Monto Ho (Harvard), Dr. D. Rubinstein (Michael Reese Hospital, Chicago), Dr. A. Iodice (University of California, Berkeley), Dr. E. A. Carusi (California Institute of Technology), Dr. J. Rothschild (Rockefeller Institute for Medical Research), Dr. J. B. Mudd (University of California, Berkeley).

GULBENKIAN FOUNDATION, LISBON

GRANTS FOR 1958

THE Trustees of the Calouste Gulbenkian Foundation, Lisbon, have announced a list of grants made during 1958 and amounting in total to nearly £1 million. The two previous lists of grants, issued in April and November 1957, totalled £1½ million. Out of this year's grants the British Isles and the Commonwealth overseas receive more than £200,000.

The list of grants includes: £42,000 to the Old Bodleian Library, Oxford, for restoring the fabric of this building, begun in the fifteenth and completed in the seventeenth century; £30,000 to Fort Jesus, Mombasa, for the restoration of the sixteenth century Portuguese fort and its conversion into a museum of East African history and archæology under the care of the Royal National Parks of Kenya; up to £6,000 over three years to the International Institute for the Conservation of Museum Objects; £1,500 to the Welsh Folk Museum for recording equipment for a survey of Welsh oral traditions of the countryside, including the domestic, agricultural and craft vocabularies, before they disappear under the impact of modern technology; £32,500 to the Centre for Nuclear Energy Research, Portugal, for equipment, and running costs for three years, for its mass spectrometry and isotope section; to the University of Coimbra, (*a*) the Chemical Laboratory, £12,430 for a spectrophotometer and expensive books, (*b*) the Physics Laboratory, £6,200 for analyser and other equipment for atomic energy research, (*c*) the Galenic School of Pharmacy, £3,020 for apparatus for electrophoresis and chromatography, (*d*) the Institute of Geophysics, £1,750 for scientific equipment; £14,375 to the Bento da Rocha Cabral Institute for Scientific Research for equipment and three years research expenses; £12,850 to the Centre for Research in Infectious Diseases, Portugal, for capital and running costs for three years; £11,250 to the Centre for Economics and Statistical Research, Portugal, over three years, for seminars and training of future research workers; £4,170 to the National Agronomy Station, Portugal, for books for the library; £3,750 to the Egas Moniz Research Centre, St. Mary's Hospital, Lisbon, for fellowships; £2,000 to the University of Lisbon Botanical Garden and Laboratory, for microfilm reader, microscopes and transport for field-work; £1,250 to the Organic Chemistry Laboratory, Higher Technical Institute, Lisbon, for equipment; £1,080 to the Hospital of Dona Estaphania, Lisbon, for scientific meetings organized by the head of the Department of Child Health.

Scholarships and other grants for education or study at home or overseas for the year 1958–59 include: £112,500 for Portuguese students and scholars, £20,000 for Armenian students, and £10,000 for scholars, research workers, etc., and £15,000 for Middle East students. In the United Kingdom £4,030 was spent in 1958.

Other grants include £50,000 to Churchill College, Cambridge, to endow three Gulbenkian studentships for graduates of universities outside the United Kingdom; up to £3,750 to the Institute of Archæology, University of Coimbra, and other archæological bodies; £3,000 to the Department of Education, Oxford, directed by Mr. Alec Peterson, to enable a study to be made of specialization in schools and its real relevance to university requirements, and then to attempt to draft an ideal syllabus and timetable for a combined arts and science sixth form; £350 a year for three years to the Egypt Exploration Society and Ashmolean Museum, Oxford, for a technician to be trained (by the reader in papyrology in the University of Oxford) in the technique of piecing together fragments of ancient papyri by matching the fibres instead of the text; £600 over two years to Prof. Christopher Hawkes (University of Oxford) for visits to Portugal at the invitation of the Ministry of National Education to collaborate with Col. Mario Cardoza of Guimarães in the excavation of early Celtic *castros* and in the training of Portuguese archæologists in the latest techniques of excavation; £700 to the Department of Economics, University of Bristol, for a study of the 'employability' of workers who have suffered long-term unemployment due to ill-health. Out of funds set aside in 1957, the Foundation has assisted one undergraduate scientific expedition this year, namely, the Westminster Hospital Medical School's expedition to the Belgian Congo. In addition, the Royal Geographical Society, London (which already lends surveying instruments to expeditions), has accepted £1,200 for a pool of other instruments and equipment for loan to university expeditions.

BIOCHEMICAL RESPONSE TO PHYSICAL INJURY

A SYMPOSIUM on "The Biochemical Response to Physical Injury" was held at Semmering, Austria, during September 7–12 under the ægis of the Council for the Organization of Medical Sciences with the assistance of the Wellcome Trust and the International Union of Biochemistry. Radiation injury was excluded from discussion.

Dr. D. P. Cuthbertson (Scotland) acted as chairman and Dr. H. B. Stoner (England) was technical secretary. The general and local arrangements were respectively in the hands of Dr. J. F. Delafresnaye (Council for the Organization of Medical Sciences) and Dr. F. G. Wewalka (Austria).

F. A. Fuhrman (United States) opened with a description of "Electrolytes and glycogen in injured tissues". He pointed out that we know more about the electrolyte pattern and its control in skin and skeletal muscle—which constitute 70 per cent of the mass of the soft tissues of the body and which are more frequently injured than other tissues—than in

any other. The main difficulty, however, is our inability to determine precisely the size of the extracellular space in injured tissue. The replacement of intracellular potassium by sodium following injury is of very great interest and appears to be due to failure of the sodium pump rather than to death of cells. It is not known how long intracellular sodium must be present to be harmful; or, indeed, whether it ever does become harmful. At least eight different enzymes are activated by potassium and inhibited by sodium. Abnormal carbohydrate tolerance has been demonstrated in potassium-deficient animals in which part of the intracellular potassium was replaced by sodium. But much more information is necessary before the electrolyte changes in complex injuries can be causally related to alterations in physiological function.

J. Trémolières and R. Derache (France), in "Metabolism of nucleotides and phosphate in injured tissue", described the uniformity of the local response to injury as exemplified by the fact that the changes in the acid-soluble phosphorus compounds go on in nearly identical ways whatever the injury (radiation excepted). There is a reduction of energy-rich compounds (phosphocreatine and adenosine triphosphate) as in anaerobic conditions. Beyond a certain point cellular lesions become irreversible. These investigators then described the state in anoxic ischæmia and of revascularization. They suggest that local œdema can be explained by a fall in the protein – adenosine triphosphate complexes which are able to select between potassium and sodium. Necrosis and irreversible proteolysis can be related to the structural functions of adenosine triphosphate in mitochondria and proteins.

"The endogenous substances inducing pathological increases in capillary permeability" were considered in two papers by A. A. Miles and D. L. Wilhelm (England), who discussed the activation of endogenous substances increasing capillary permeability (Miles), and the evaluation of the role of endogenous permeability (Wilhelm). They emphasized that among the early responses to injury, the inflammatory reaction is paramount. In their view, in our present state of knowledge it is almost impossible to analyse the factors operative in a long-lasting and severe inflammation, and progress in this field is most likely to be achieved by studying the essential reactions of inflammation induced by minimal stimuli. Judging from the large number of relatively simple substances which can increase permeability, it is possible that the tissues use one or several of a variety of endogenous substances as mediators, and that these differ according to the type of injury. In certain circumstances and certain animals, histamine and 5-hydroxytryptamine appear to be mediators. These workers could not subscribe to the view that, since endogenous leukotaxine, globulin permeability factor and so forth are there, they must in consequence play some part in permeability changes, otherwise they would not be there. Their view is that even supposing all endogenous substances in the body have their proper and necessary role in the living tissues, the biological activities in terms of which we choose to identify and explore them may be wholly irrelevant to the function they fulfil in the body.

A. Fonnesu (Italy) described "Changes in energy transformations as an early response of the cell to injury". The well-known histological picture of cloudy swelling is the morphological result of these changes—a condition described by Rudolph Virchow in 1871 as a kind of acute hypertrophy with tendency to degeneration. The features of this condition are as follows: (1) an alteration of the mitochondria which follows, or is followed by, a partial inhibition of phosphorylation coupled with oxidation; as a consequence, aerobic glycolysis increases; (2) increased protein synthesis. Assuming the mitochondrial alteration is the first response of the cell to injury, this may be the cause of an increase of aerobic glycolysis and an increase of inhibition. No answer can be given as to how impairment of oxidative phosphorylation can lead to an enhancement of an endoergonic process such as protein synthesis. Other conditions, in pathology, are known in which the uncoupling of oxidative phosphorylation is accompanied by an increase of both glycolysis and protein synthesis.

Concerning the more general response to injury, "The effect of limb ischæmia on carbohydrate distribution and energy transformation" was analysed by H. B. Stoner and C. J. Threlfall (England). It appears that during the period of limb ischæmia and for the first part of the survival period afterwards, the brain, liver, heart and uninjured muscle are adequately oxygenated and the metabolic changes in these organs cannot be attributed to hypoxia. The secretion of the adrenal medulla in response to the injury is the main cause of the altered carbohydrate distribution. The mechanism of the changes in energy transformations which occur at this time is not yet understood.

In the estimation of these investigators the ability of the animal to withstand the injury is probably decided during this early period and it is possible that the biochemical changes which occur are part of a defensive mechanism. If the animal is unable to withstand the injury, oxygen transport fails during the later part of the survival period and the resulting tissue hypoxia leads to the terminal changes in energy (heat) production and carbohydrate metabolism.

A. G. B. Kovách (Hungary), in a paper on "Metabolic responses to injury in the cerebral tissues", described the favourable effect of perfusion of the brain with normal blood in hæmorrhagic and ischæmic shock. The functional changes as tested by electrocorticographic investigations support the hypothesis that impairment of the nervous system plays an important part in the development of shock. The oxygen consumption of the brain—its oxygen requirement—does not decrease during shock, in fact it rises, in spite of the fact that the circulation in the head is deficient. Unlike muscle where the glucose uptake is lessened after shock, the brain remains unchanged in this respect, to the terminal stage, when it diminishes. The hexokinase activity in the brain of the animal in shock increases, whereas in muscle it is slowed up. On the other hand, cerebral anoxia (stagnant or arterial) lowers the brain hexokinase activity. These and other changes—particularly in phosphorus compounds—might be attributable to an increase in intracellular potassium ions. The mechanism of this can only be determined by further experiment.

R. Fåhraeus (Sweden) described the "Tissue injury due to the reduced filtrability of the erythrocytes". The intravascular aggregation of the erythrocytes in rouleau formation (termed by Knisely 'sludging') implies a mechanism which is advantageous for the circulation of the blood in certain aspects of the vascular system. This aggregation of the

erythrocytes favours their transport at the expense of the plasma and decreases the relative viscosity of the blood. But such rouleau formation may give rise to circulatory disturbance.

Determination of the filtrability of the erythrocytes at different blood pressures indicates that a large fall in blood pressure must have a more serious prognosis when the suspension of the blood is strongly reduced. In clinical cases with great aggregation of the erythrocytes the circulation *sub finem vitae* ceases earlier.

In reviewing the "Effect of physical injury on lipid metabolism", E. J. Masoro (United States) dealt mainly with the effects of cold injury and the interrelationship of energy generation and the intermediary metabolism of lipids. At the moment the greatest barrier to the understanding of the effect of physical injury on lipid metabolism is still the absence of certain key data.

D. P. Cuthbertson (Scotland) contributed by discussing "The disturbance of protein metabolism following physical injury". He pointed out that the increased metabolism and urinary excretion of nitrogen, sulphur, phosphorus, potassium and creatine are the main energy and material losses to the body following moderate to severe physical injury such as the fracture of a femur. These alterations in catabolism reach their peak about the third to eighth day in man. There is also generally a slight rise in body temperature and pulse-rate. Comparable changes in nitrogen metabolism are found in the rat, sheep and, as Needham has shown, even in Crustacea. This rise in the surviving organism succeeds an initial depression of vitality following receipt of the wound. In the animal depleted in protein there is no increase in protein catabolism and in heat production following injury. The degree of response is related to the previous nutritive state.

Injury to an animal leads to lessened activity and lessened activity usually results in a diminished food and water intake. The necessity to heal is urgent and Dr. Cuthbertson's view is that the injury done sets in motion a chain of events to meet both the exigencies of repair and of maintenance. This involves changes which may even affect the internal milieu. The rise in heat production which is traceable to the protein oxidized will undoubtedly affect the rates of biochemical reaction.

A. Pekkarinen (Finland) gave a well-documented account of "The effect of operation and physical injury on the adrenal glands and the vegetative nervous system in man". The excretion of adrenaline, noradrenaline and total 17-hydroxycorticosteroids increases markedly after certain operations, thus showing a close relation between the vegetative nervous system and the pituitary-adrenocortical system, at least functionally. The rises might be regarded as of therapeutic benefit, promoting the adaptation of the organism to the stress of operation. The highest urinary excretions of noradrenaline and adrenaline correspond to liberation of 5 mgm. noradrenaline and 8·4 mgm. adrenaline. In most patients the excretion of these substances becomes normal during the first three days after operation. It may also be assumed that the secretion of steroids by the suprarenal cortex may decrease owing to the increased circulatory 17-hydroxycorticosteroid inhibiting the secretion of adrenocorticotrophic hormones from the pituitary gland.

An interesting finding is the significantly higher excretion following injury of adrenaline, noradrenaline and total 17-hydroxycorticosteroids in men compared with women.

The part played by aldosterone secreted by the adrenal cortex in the regulation of the humoral equilibrium during operations is yet unknown.

"Fluid, electrolyte, and plasma protein disturbance in shock" were dealt with by R. C. Millican (United States). He pointed out that this kind of study is important, for circulatory collapse occurs in normal animals in which there are losses of fluid, electrolyte, and protein to the extent observed in shock arising from hæmorrhage or swelling at the site of physical injury. Under certain conditions death from shock can be prevented by administration of fluids, electrolytes, and proteins. In untreated shock associated with a swelling of the injured areas of about 4–5 per cent of body weight, the fluid accumulation within the injured area occurs at the expense of the injured tissues.

The total sodium accumulation in the injured area of mice following application of a tourniquet to the hind legs is equivalent to the entire sodium in the circulating blood, or approximately 25 per cent of the extracellular fluid.

Dr. Millican considered that as substantial amounts of potassium were liberated from injured tissues this was an important factor in shock when combined with the fluid and sodium loss. Doubt is cast on the importance of plasma protein in shock in mice by the lack of effectiveness of protein solutions when administered in the absence of electrolytes. Survival response is closely related to the sodium content of the administered fluid.

V. Wynn (England) took up one aspect of the clinical side in his paper on "Some problems of water metabolism following surgery". He considers that the common finding of a low plasma osmolarity for several days after the trauma is explained by water retention in excess of electrolytes. Since renal function may be otherwise normal, present evidence suggests persistent antidiuretic hormone secretion as the cause of the oliguria. It seems that the supra-optic-hypophyseal system is made more sensitive in some way by trauma, so that a variety of stimuli provoke secretion of antidiuretic hormone ; and the primary function of osmo-regulation by the system is seriously impeded or lost. An inhibitory effect upon aldosterone production is a secondary consequence of the water retention. This leads to renal loss and aggravates the hypotonicity of the body fluids.

In a discussion on the "Influence of environment on the metabolic response to injury" R. E. Haist (Canada) described his experiments, which indicate a prolongation of the survival time of rats, previously exposed to cold, and shocked by a clamping technique, over controls not so exposed. An increased blood volume due to the exposure may also be a factor. Sodium is retained by such cold-acclimatized animals. Previous cold-acclimatization does not alter the changes in muscle chemistry and temperature during and following ischæmia, or the hepatic blood flow after ischæmia, but does lead to a lesser hepatic temperature.

It was clear from H. Smith's (England) account of the "Biochemical response to bacterial injury" that infection with a number of bacteria and injection of different bacterial products can lead to a response in the host physiologically and biochemically similar to that produced by physical injury. The stimulus to this response appears to be a loss of circulating

blood volume either from extravasation into tissue spaces locally or generally, for example, in shock produced by anthrax, or from a peripheral pooling of the blood and a decrease in venous return as, for example, in shock produced by staphylococcal and meningococcal toxins. The possible biochemical mechanisms whereby different bacterial products affect blood vessels is a relatively untouched field for research.

W. W. Spink (United States), in his paper on "Brucellosis as a model for metabolic studies on bacterial shock and inflammation," directed attention to the increasing interest shown in recent years in the peripheral vascular collapse caused by endotoxins of Gram-negative bacteria. There is vasoconstriction of the small vessels, which causes ischæmia of the tissues, and changes in cellular function result. This is followed by vasodilation and stagnation of blood, increased vascular permeability, and œdema and hæmorrhage. There is reduced cardiac output because of peripheral pooling of blood. Renal failure occurs because of the compensatory vasoconstriction, which results in ischæmic tubular necrosis.

The metabolic response of the host to bacterial invasion includes alterations in hormonal activity. The adrenal cortex is stimulated, as reflected by increased concentrations of adrenocorticoids, especially cortisone. The thyroid stimulates the activity of the adrenal cortex. Some doubt was expressed as to the wisdom of giving the large amounts of exogenous corticosteroids advised by Dr. Spink during the initial critical period of endotoxin shock. It was of interest that he had found that triiodothyronine accelerated the lethal action of endotoxin.

"The bacterial factor in traumatic shock" was discussed by J. Fine, E. D. Frank, H. A. Ravin, S. H. Rutenburg and F. B. Schweinburg (United States), who found evidence of a toxin appearing in the blood of animals in hæmorrhagic shock, such toxin having many of the hallmarks of a bacterial endotoxin. They consider that it is the cause of the irreversibility to transfusion in their standardized preparations. A toxin with similar properties to the one in the blood in hæmorrhagic shock is apparently present in the blood of the animal in tourniquet shock and in non-bacteræmic septic shock. The source of this toxin appears to be such Gram-negative bacteria as may be present in the animal's tissues, and the endotoxins normally present in the gastro-intestinal tract, which appear to enter the circulation at a steady rate, if only in trace quantities. It is thought that when shock, however produced, becomes unresponsive to therapy, the refractory state of the peripheral vessels is due to unneutralized endotoxins through impairment of the reticulo-endothelial system. The protective effect of reserpine and of dibenamine given prophylactically lend strength to the view that the endotoxins act adversely on these vessels by intensifying the local action of adrenaline or noradrenaline.

S. M. Rosenthal and H. Tabor (United States), in their paper on "Some aspects of therapy of injury", described the survival effects of administering isotonic sodium salts to mice subjected to what would otherwise be one lethal dose of burn trauma, tourniquet trauma or hæmorrhage. In their estimation, sodium and fluid depletion are the major factors in the cause of shock. Saline or plasma in amounts of 5 per cent of body-weight (50 ml./kgm.) is inadequate. These authors have been able to demonstrate a specific effect from the sodium ion in shock. Potassium salts behave in an opposite manner to sodium and are quite toxic. In shocked mice there is an eightfold increase over the toxicity in normal. Glucose and colloid solutions containing no sodium were relatively ineffective in the therapy of shock. The concept that plasma proteins exert their osmotic effects by being held rigidly in the vascular bed must be modified by the demonstration of Wasserman and Mayerson in 1952 that a complete extravascular circulation of the plasma proteins occurs every 20 hours.

In hæmorrhage and hæmorrhagic shock where there is a large loss of red cells, the striking efficacy of administering red cells has been clearly demonstrated, but there is little evidence to substantiate its value in shock from burn or other local trauma. In experimental burns and tourniquet shock whole blood is no more effective than plasma or saline solutions.

In studies on burned children in Peru a small but statistically significant benefit from plasma above that from saline was observed. The important problem of late deaths following severe burns is also being studied in Peru by Drs. Rosenthal and Millican.

This, the first main symposium covering this field of investigation to be held in Europe since the Second World War, was of great value to the participants. The papers contributed and the discussion which followed will be published in due course by Blackwell Scientific Publications, Ltd.

D. P. Cuthbertson

FREE RADICAL STABILIZATION

Free radical chemistry began with the discovery of the stable aromatic free radicals by Gomberg in 1900. The second stage of the subject developed more gradually as the occurrence and importance of unstable free radicals became increasingly apparent and as kinetic and spectroscopic methods for their study in the gas phase and in solution were perfected. During the past few years a third chapter in free radical chemistry has been opened with the realization that even the most reactive of radicals can readily be stabilized for indefinite periods by trapping them in a rigid matrix at low temperatures.

An informal discussion of the Faraday Society on this subject was held in the Chemistry Department of the University of Sheffield on September 4 and 5. The meeting was attended by about one hundred and eighty scientists, half of whom were from Britain, fifty from the United States and Canada, and forty from other countries. Twenty-one papers, covering nearly all aspects of the subject, were presented and discussed.

The three principal methods of preparation of stabilized radicals are: (1) by irradiation of a rigid solid or solution at low temperatures; (2) by elec-

trical or thermal dissociation of a gas and subsequent trapping on a cold surface; (3) by chemical reaction in a rigid or viscous medium, for example, polymerization.

The trapped radicals are then investigated by physical methods, the most useful being absorption spectroscopy in the infra-red, visible or ultra-violet regions, thermal analysis and electron paramagnetic resonance spectroscopy. The latter method is particularly appropriate, and it is fortunate that it was developed at about the same time as methods for the stabilization of radicals.

Practically every type of radical has now been stabilized by one of these methods, from atoms and diatomic radicals to complex odd-electron molecules in polymeric and biological systems. Although the subject is at an early stage of development, the identification of many of these radicals is now quite certain. The simplest of all—the hydrogen atom—is readily prepared and identified by means of its characteristic electron spin resonance doublet, and detailed studies of its formation by gamma irradiation of acid solutions at 77° K. were reported by R. Livingston, H. Zeldes, A. Weinberger and R. Holmberg (Oak Ridge National Laboratory). The isolation of other atomic species is less well established. Unstable products are undoubtedly present in the condensed products of an electrical discharge through nitrogen or after γ-irradiation or electron bombardment of the solid at 4° K. (E. M. Hörl, National Bureau of Standards, Washington), but the evidence at present suggests that, although nitrogen atoms have been detected, N_3 may be the main constituent under some conditions (L. A. Wall, D. W. Brown and R. E. Florin, National Bureau of Standards; also K. Jen, Johns Hopkins University, Maryland).

The first work on the stabilization of simple inorganic free radicals was that of F. O. Rice (Catholic University, Washington), who found a transient blue substance, attributed to the imine radical, in the condensed products of dissociation of NH_3. Rice illustrated this early experiment, as well as later work, by means of excellent colour films which he recommended as being more reliable than the actual experiment for demonstrations of this kind. G. Wilse Robinson and M. McCarty (Johns Hopkins University, Baltimore) reported some very interesting and successful work on the stabilization of diatomic and triatomic radicals at 4° K. The radicals NH, OH, CH, C_2, NH_2, HNO, HCO and CNO, prepared in the electrical discharge, have been positively identified in a rigid argon matrix by means of their electronic absorption spectra. The spectra are surprisingly sharp and reveal that radicals such as NH_2, NH and OH experience nearly free end-over-end rotation in the matrix.

Most successful work on the aliphatic radicals has utilized electron spin resonance methods since their electronic spectra lie in the far ultra-violet, and infra-red methods present many problems. For example, H. W. Brown (National Bureau of Standards) was not able to obtain the infra-red spectrum of methyl by photolysis of methyl iodide, but K. Jen successfully used this method to record its electron spin resonance spectrum. M. S. Matheson (Argonne National Laboratory) summarized the radicals which have so far been identified in the irradiation products of paraffins, alcohols, ethers, aldehydes, ketones, fatty acids and other aliphatic compounds. The electron spin resonance spectra of the simple alkyl radicals are now well established. The ethyl radical is formed by the γ-irradiation not only of ethane but also of ethylene, and R. Klein and M. D. Scheer (National Bureau of Standards) described studies of the reactions of hydrogen atoms with solid olefins at 77° K. which show that addition occurs readily under these conditions. The γ-irradiation of alcohols and ethers is very specific in removing almost exclusively the hydrogen atom from the carbon α to the oxygen. D. J. E. Ingram and M. C. R. Symons (University of Southampton) described how the same radicals are also formed by photolysis of a solution of hydrogen peroxide in the rigid alcohol; the OH radical first formed readily abstracts hydrogen from the alcohol at 77° K.

For the aromatic radicals electronic absorption spectroscopy has proved to be most useful. H. T. J. Chilton G. Porter (University of Sheffield) and E. E. Strachan (British Rayon Research Association) described the preparation and stabilization of a variety of such radicals both by photolysis and by gamma radiolysis of rigid solutions at 77° K. In the case of the ionizing radiations the dissociation of the aromatic molecules is brought about almost exclusively by transfer of energy absorbed by the solvent.

The irradiation of polymers leads to larger radicals, and these are often still present at normal temperatures. For example, V. V. Voevodsky (Academy of Sciences, U.S.S.R.) described electron spin resonance studies of radicals trapped in irradiated polytetrafluoroethylene at 77° K., some of which remain when the specimen is warmed to 20° C. Radicals are also trapped in polymers as a result of the polymerization reaction itself and are responsible for unusual and characteristic kinetic behaviour. C. E. H. Bawn, T. P. Hobin and W. J. McGarry (University of Liverpool) described studies of trapped radicals in acrylonitrile, vinyl chloride, styrene and vinylidene chloride.

The general occurrence of stabilized radicals in polymeric and biological systems was reviewed by C. H. Bamford and A. D. Jenkins (Courtaulds, Ltd., Maidenhead). Electron spin resonance measurements have shown that metabolically active plant and animal tissues such as leaves, roots, seeds, blood, muscle and liver have a remarkably high radical content, and W. Gordy (Duke University) described recent investigations on such systems. Their function and the means by which they are stabilized and, indeed, their chemical nature are little understood as yet. J. L. Vivo-Acrivos and M. S. Blois (Stanford University, California) reported on electron spin resonance studies of stable radicals in natural and synthetic melanins. D. K. Ghosh and D. H. Whiffen (University of Birmingham) described their detailed work on the electron spin resonance spectra of radicals trapped in a single crystal of glycine after gamma irradiation. It can be shown that the radical is $+NH_3.CH.COO^-$. The spectrum is anisotropic and shows far more detail than that from a polycrystalline material. The arrangement of the trapped radicals has the same symmetry as that of the molecules in the host lattice.

Although the major effort in the field of radical stabilization is at present directed towards the identification of the trapped species, it is clear that, once the spectra have been assigned, the method will provide a powerful means of investigation in many fields, and particularly of the primary processes of photochemistry, radiation chemistry and the electrical discharge. Masterly reviews of these three

aspects of the subject were given by H. Linschitz (Brandeis University), M. S. Matheson and H. P. Broida. There was considerable discussion of the characteristic behaviour of excited states in rigid media, and Broida stressed the need for more information about the matrix structure and about the fundamental limitations to trapped radical concentrations.

There has been a great deal of interest in the possible use of stabilized radicals as high-energy rocket propellants. The important quantity to be considered is the heat of reaction per gram, and there seems little hope of increasing this greatly above 3 kcal./gm. with conventional molecular fuels. If pure atomic hydrogen could be utilized, the heat of reaction would be 51·2 kcal./gm., but the present indications are that concentrations which can be trapped are limited to 1 per cent or less. Other, heavier radicals are all much less suitable, and G. C. Szego (General Electric Co., Cincinnati) concluded that, at present, this application of stabilized radicals is not promising. Some enthusiasm was shown about the possibility of utilizing metastable excited states, such as the triplet state of helium, which has an excess energy of 113 kcal./gm.

Special experimental techniques are mainly concerned with the adaptation of existing methods to low temperatures. L. J. Shoen, L. E. Kuentzel and H. P. Broida (National Bureau of Standards) described glass Dewar flasks for optical studies at low temperatures, P. Le Goff and L. P. Blanchard (University of Nancy) described a mass spectrometer with a low-temperature ionization chamber, and H. S. Peiser (National Bureau of Standards) gave an account of his very elegant X-ray crystallographic studies on low-temperature solids.

The enthusiasm of the discussions was typical of a field where new phenomena are found in nearly every experiment which is performed. The international character of the meeting was a very pleasant feature, and this was assisted by financial support from the United States Department of the Army through its European research office.

George Porter

NEW POTENT REACTIVATORS OF ACETOCHOLINESTERASE INHIBITED BY TETRAETHYL PYROPHOSPHATE

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CERTAIN organophosphates, for example, tetraethyl pyrophosphate (TEPP), di*iso*propyl phosphonofluoridate (DFP), diethyl *p*-nitrophenylphosphate (*E* 600), and a number of widely used insecticides and their metabolites, are potent inhibitors of acetocholinesterase. Organophosphate poisoning (fatal when sufficient acetylcholine has accumulated in the body) has been reported from many countries, especially from Japan[1] and the United States[2], and an efficient treatment has become essential. Acetocholinesterase is reputed to possess positively and negatively charged regions, commonly called anionic and esteratic sites, which participate in the hydrolysis of acetylcholine. In the inhibition process, a dialkylphosphoryl group, or some related group, becomes attached to the esteratic site and in this way deprives the enzyme of its hydrolytic function[3]. Spontaneous reactivation of diethyl phosphoryl-acetocholinesterase occurs very slowly, but the formation of di*iso*propyl phosphoryl-acetocholinesterase is, for all practical purposes, irreversible[4].

Certain nucleophilic reagents restore the activity of freshly phosphorylated acetocholinesterase by displacing the phosphoryl group from the enzyme[3]. Hitherto, pyridine-2-aldoxime methiodide has proved, in general, to be the most potent reactivator, and attachment of its quaternary nitrogen to the anionic site of the phosphorylated enzyme has been considered to contribute to its potency[5].

During the past two years we have synthesized a large number of oximes and studied the affinity of these compounds for acetocholinesterase, their interaction with tetraethyl pyrophosphate, and their effectiveness in restoring the activity of acetocholinesterase inhibited by tetraethyl pyrophosphate. The compounds can be classified roughly as aliphatic oximes, and compounds related to pyridine, indole, indolinene, quinoline and *iso*quinoline. The most powerful reactivators that have so far emerged are structurally related to pyridine, the effectiveness of some of these being shown in Tables 1 and 2. Monoximes and dioximes of *bis*-pyridinium ions (compounds 12–18; Table 2) are all considerably more potent reactivators than pyridine-2-aldoxime methiodide (*P*-2-*AM*) although they are derivatives of the less active pyridine-4-aldoxime methiodide (*P*-4-*AM*). A considerable gain in activity is also obtained by terminal halogen substitution in the alkyl side-chain (compare compounds 3 and 8). Table 2 shows that the reactivating power of the oximes cannot be predicted from their hydrolytic activity and their affinity for the anionic site of acetocholinesterase. The order of activities found:

$$P\text{-}2\text{-}AM > P\text{-}4\text{-}AM \gg P\text{-}3\text{-}AM$$

is in conformity with unpublished results obtained with other compounds, which suggests that a conjugative connexion between the quaternary nitrogen and an oxime or hydroxamic acid group is an essential feature for high activity.

All the compounds in Table 2 have been subjected to a preliminary screening for antidotal properties.

TABLE 1

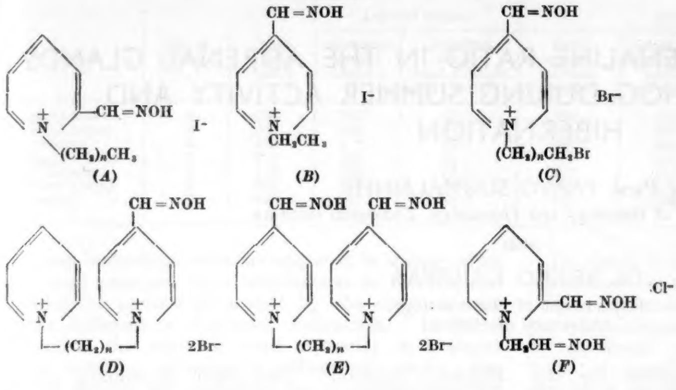

TABLE 2. *In vitro* REACTIVATION OF HUMAN ACETOCHOLINESTERASE INHIBITED BY TETRAETHYL PYROPHOSPHATE

No.	Oxime	Melting point (°C.)	*A* Potency as reactivator	*B* Calculated value for *A*	*C* Ratio $\frac{A}{B} \times 100$
1	*P-2-AM*	225	100	100	100
2	*P-3-AM*	156	0·03	11	0·27
3	*P-4-AM*	179	6	26	23
	(*A*)				
4	$n = 1$	180	54	210	26
5	$n = 2$	192	63	560	11
6	$n = 3$	168	87	6,780	1·3
7	(*B*)	152	3	18	17
	(*C*)				
8	$n = 0$	245	160	80	200
9	$n = 2$	165	190	750	25
10	$n = 3$	144	25	790	3·2
11	$n = 4$	164	94	160	58
	(*D*)				
12	$n = 3$	225d	800	42	1,900
13	$n = 4$	235d	670	21	3,200
14	$n = 5$	195	750	87	8,600
	(*E*)				
15	$n = 2$	310	1,700	110	1,500
16	$n = 3$	239d	2,200	95	2,400
17	$n = 4$	240d	1,800	100	1,800
18	$n = 5$	209d	1,600	740	210
19	(*F*)	196	20	220	9

Washed human red cells were used as enzyme source and results obtained with *P-2-AM* were taken as 100. *B* is the affinity of the oxime for acetocholinesterase × rate of interaction of the oxime with 2×10^{-8} *M* tetraethyl pyrophosphate. All experiments were carried out at 37° C. with 0·01 *M* acetylcholine chloride as substrate in a medium of 0·025 *M* sodium bicarbonate equilibrated with 95 per cent nitrogen + 5 per cent carbon dioxide. The method for determining *A* was in principle that described previously (ref. 9), except that reactivation was allowed to proceed in the centre of the manometric vessel for 30 min. before addition of the substrate.

Table 3. PROTECTION BY OXIMES AGAINST LETHAL TETRAETHYL PYROPHOSPHATE POISONING

Compound	No. of mice surviving for 24 hr./No. of mice injected					
	µgm. Tetraethyl pyrophosphate injected per mouse					
	8	16	32	64	128	256
—	5/6	0/8	0/6	0/6	0/6	0/6
P-2-AM	—	0/6	0/18	0/4	—	—
12	—	4/4	3/6	1/4	—	—
13	—	—	5/6	1/4	—	
14	—	—	5/6	4/4	3/5	0/5
15	—	4/4	2/6	1/4	—	—
16	—	—	6/6	4/4	5/5	7/15
17	—	—	6/6	4/4	4/5	0/5

Compounds were administered in amounts equimolar to 0·5 mgm. *P-2-AM* per mouse. Male white mice weighing between 18 and 20 gm. were injected intraperitoneally with 0·2 ml. of the oxime in 0·9 per cent sodium chloride solution and then 5 to 8 min. later they were injected subcutaneously with 0·2 ml. tetraethyl pyrophosphate in 0·9 per cent sodium chloride solution. Mice injected with the oximes alone showed no visible changes.

As can be seen from Table 3, under the experimental conditions chosen, some oximes and dioximes of *bis*-pyridinium ions are markedly superior to pyridine-2-aldoxime methiodide as antidotes to tetraethyl pyrophosphate *in vivo*. If tolerated satisfactorily, they will be considerably superior to pyridine-2-aldoxime methiodide in restoring the activity of acetocholinesterase in human beings poisoned by organophosphates. This is of great potential importance since most of the new compounds listed in Table 3 are more soluble and appear to be more stable than pyridine-2-aldoxime methiodide, and also in view of the reported observation that 1 gm. of the latter, injected intravenously, restores the activity of erythrocyte acetocholinesterase in human beings poisoned with parathion, but has only a disappointingly small influence on the phosphorylated enzyme formed by other organophosphates[6].

It might be expected that oximes of relatively low toxicity which, in relation to pyridine-2-aldoxime methiodide, have a higher affinity for acetocholinesterase or hydrolyse tetraethyl pyrophosphate more rapidly, would protect animals against lethal tetraethyl pyrophosphate poisoning to a greater extent than pyridine-2-aldoxime methiodide. Compounds 6, 9 and 10 have a 64-, 17- and 22-fold higher affinity than pyridine-2-aldoxime methiodide for acetocholinesterase, and compound 8 is 2·6 times more effective than pyridine-2-aldoxime methiodide in hydrolysing tetraethyl pyrophosphate. However, under the experimental conditions of Table 3, compounds 6, 8, 9 and 10 failed to protect mice from a lethal dose of 32 µgm. tetraethyl pyrophosphate.

A complete account of this work is to be published elsewhere. While this work was in progress, two reports[7,8] have appeared describing the reactivating and the antidotal effect of compound 16 in animals poisoned with sarin. Discrepancies between the findings of these authors and the results presented here probably arise from differences in the type of phosphorylated enzyme.

Should the results obtained with compound 16 be applicable to other species, pyridine-2-aldoxime methiodide becomes obsolete as an antidote for tetraethyl pyrophosphate poisoning. Since many of the insecticides used at present form diethylphosphoryl-acetocholinesterase, there is a good chance that compound 16 will be highly effective in many cases of accidental organophosphate poisoning which are frequently reported.

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ADRENALINE/NORADRENALINE RATIO IN THE ADRENAL GLANDS OF THE HEDGEHOG DURING SUMMER ACTIVITY AND HIBERNATION

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WE have recently published figures for the adrenaline and noradrenaline content of the adrenal glands of the hedgehog during the summer[1]. The adrenal glands of the active hedgehog with a normal body temperature contain considerable amounts of noradrenaline, the values being 40 per cent of the total catechol amine content in the male, and rather less in the female. With regard to the adrenaline/noradrenaline ratio, the hedgehog belongs to the same type as the cat family.

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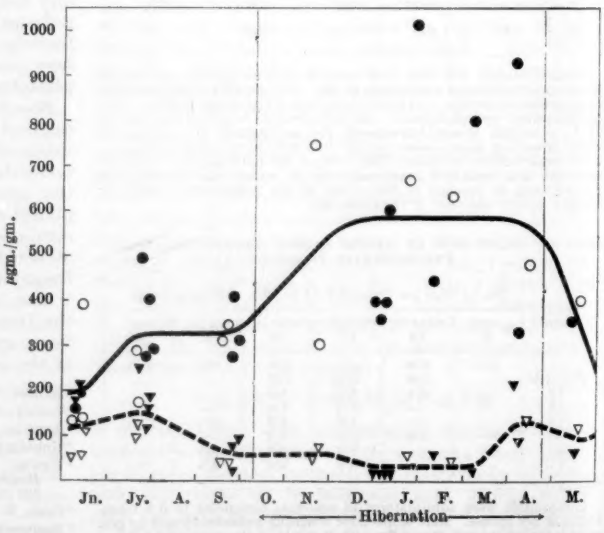

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Season	No. of animals	Body-weight (gm.)	Adrenal weight		Catechol amines				Condition
			Absolute weight (mgm.)	Relative weight (mgm./100 gm. body-weight)	Total (μgm./gm. adrenal weight)	Adrenaline (μgm./gm. adrenal weight)	Noradrenaline (μgm./gm. adrenal weight)	Noradrenaline per cent	
Early summer	5	560	389	69·5	320	199	121	37·8	Awake
Midsummer	6	650	305	46·9	493	338	155	31·4	
Autumn	4	458	253	55·2	387	332	55	15·0	
Early winter	2	378	231	61·1	587	526	61	10·4	
Midwinter	9	498	239	48·0	617	585	32	5·2	Hibernating
Early spring	3	385	218	56·6	713	576	137	19·2	
Spring	2	645	267	41·4	462	380	82	17·7	Awake

When hedgehogs were investigated in spring, after they had emerged from hibernation in Nature, the histological picture presented by the adrenals was rather different in different individuals. In some specimens the adrenals were evidently in a slight alarm reaction, whereas in others the cortex was slightly active. By the end of May or in the beginning of June, the function of the cortex seemed to have become normal.

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The question of what factors are responsible, despite the increase in the adrenaline content of the adrenals, for the various special features of the hedgehog's hibernation, such as the marked bradycardia, hypoglycæmia and steady glycogen content of the liver and muscles throughout hibernation[3,4], will be discussed elsewhere.

Table 2. RELATIVE PHOTOCELL INDICES FOR HISTOCHEMICAL DETERMINATIONS OF THE TOTAL CATECHOL AMINES AND NORADRENALINE IN THE ADRENAL GLANDS OF THE HEDGEHOG

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When the animal awakes from hibernation and becomes homoiothermic again, the rewarming of the anterior half of the body takes place much more rapidly than that of the posterior half[8,9]. Lyman and Chatfield have shown[9] that vasoconstriction takes place in the vessels of the posterior part of the body and in the intestines caudal to the liver. The blood then circulates only in the anterior part of the body. All the heat produced by the heart and the muscles of the anterior trunk serves to warm the front half of the body. What connexion may exist between the variation in the noradrenaline and adrenaline content, in addition to any other possible vasoconstrictory substances, and such changes in vasoconstriction and vasodilation is still unknown.

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ADRENALINE/NORADRENALINE RATIO IN THE ADRENAL GLANDS OF THE HEDGEHOG DURING SUMMER ACTIVITY AND HIBERNATION

By Prof. PAAVO SUOMALAINEN
Department of Histology and Physiology, Zoological Institute
AND
Dr. VEIKKO J. UUSPÄÄ
Department of Pharmacology,
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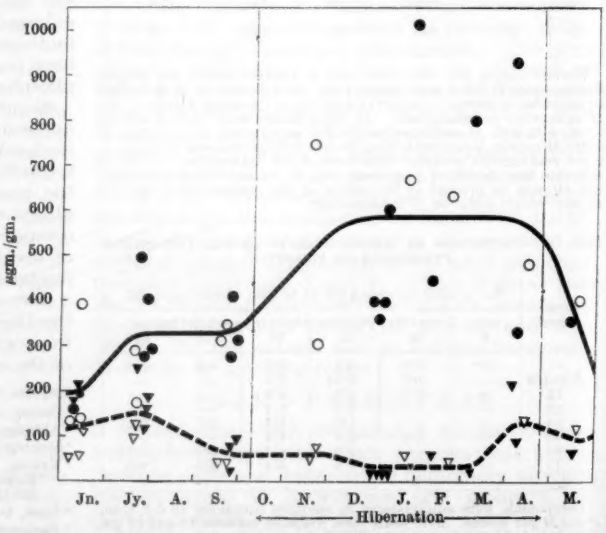

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HYPERCHROMICITY AND NUCLEIC ACIDS

By Dr. A. M. MICHELSON
Arthur Guinness, Son and Co. (Dublin), Ltd., Dublin, Ireland

DEGRADATION of ribonucleic acids by alkali, ribonucleases and other reagents, and of deoxyribonucleic acids on treatment with deoxyribonucleases or on denaturation, is accompanied by an increase in ultra-violet absorption, normally measured in the region of 260 mμ, the absorption maximum for nucleic acids. In view of the profound importance of the anomalous ultra-violet absorption characteristics of nucleic acids in relationship to the fine structure of the macromolecule, the hyperchromicity of a number of relatively simple polynucleotide derivatives was studied. It should, perhaps, be emphasized that, except as otherwise described, the specimens used were synthetic[1] and as such contained a mixture of 3′ : 5′ and 2′ : 5′ internucleotide linkages, in contrast to natural and biosynthetic polymers, which have 3′ : 5′ linkages exclusively. The results are given in Table 1. Contrary to statements in the literature[2] that hyperchromicity is not due to the simple union of a few mononucleotides, it can be seen that appreciable values are obtained even for dinucleotide derivatives, in agreement with the observations of Sinsheimer[3] and of de Garilhe and Laskowski[4] that small oligodeoxynucleotides have about a 10 per cent hyperchromic effect. Thus, even a simple dinucleoside phosphate—adenosine-2′ uridine-5′ phosphate[5]—exhibits a hyperchromicity of 12·8 per cent (as does the analogous adenosine-2′(3′) thymidine-5′ phosphate[5]), whereas in the polyadenylic series, hyperchromicity rapidly reaches a limiting value of approximately 35 per cent at chain lengths of 5–6.

In view of the zero hyperchromicity of polyguanylic acids at alkaline *p*H's, the variation of hypochromicity with *p*H was examined for a number of derivatives (Table 2). The results indicate that while ionization of the purine or pyrimidine moiety has a pronounced effect in certain cases, hydrogen bonding between the bases cannot be accepted as a cause of hyperchromicity in simple nucleotide derivatives.

Table 1

Compound	Average chain length	$\lambda_{max.}$ in 0·2 *N* sodium hydroxide		Alkaline hyperchromicity
		Polymer (mμ)	Products (mμ)	
A 2′(3′)P	—	—	259·5	0
Diadenylic acid	—	258·5	259·5	15·1
Triadenylic acid	—	258	259·5	22·8
Tetraadenylic acid	—	258	259·5	30·7
Pentaadenylic acid	—	258	259·5	32·9
Polyadenylic acid	7·7	258	259·5	31·8
Polyadenylic acid	13·6	257·5	259·5	36·7
Polyuridylic acid	6·6	261	261	6·5
Polyuridylic acid	11·9	261	261	8·6
Polyguanylic acid	5·4	260–266	260–266	0
Polyguanylic acid	12·5	260–266	260–266	0
A 2′P5′U	—	261	260	12·8
A 3′P5′C3′P (from RNAase digest)	—	262	262	7·2
Synthetic RNA	12·5	260	261	14·3
Yeast RNA	12·2	260	261	12·0
RNAase-resistant cores	6·2	259	260	10·9
PolyAU (4·5 : 1) random	5·2	259	260	21·1
PolyAU (1·4 : 1) random	3·8	259·5	261	18·4
PolyAU (3·1 : 1) tracts	5·3	259	260	22·9
PolyAG (1·9 : 1) random	6·2	258	260	19·0

Key: A, adenylic acid; U, uridylic acid; G, guanylic acid; RNAase, ribonuclease; RNA, ribonucleic acid; P, phosphate.

Table 2

Acid	Hyperchromicity		
	0·01 *N* hydrochloric acid	Water (*p*H 7)	0·2 *N* sodium hydroxide
Diadenylic	0	—	15·1
Triadenylic	6·8	—	22·8
Tetraadenylic	13·2	—	30·7
Pentaadenylic	16·4	—	32·9
Polyadenylic (13·6)	22·9	—	36·7
Polyguanylic (3·2)	9·0	10·3	0
Polyguanylic (5·4)	14·6	16·5	0
Polyguanylic (12·5)	18·0	23·0	0
Polyadenylicguanylic (6·2)	14·7	36·7	19·0
A2′P5′U	12·3	16·0	12·8

While the results for polyguanylic acid are possibly an extreme example of the variation of hyperchromic effect with *p*H, it is clear that the effect of *p*H on the ultra-violet absorption of a large nucleic acid, relative to that of its component mononucleotides, will be a composite of many different curves, characteristic not only of the nucleotide composition but also of the order of bases in the polymer. The hyperchromic effect on degradation of the polymer is likewise a function not of any particular tract of nucleotides but of the total molecule determined by both the composition and order of the various bases.

It may be noted that in addition to the reduction in ultra-violet absorption there is also a small hypsochromic shift accompanying polymer formation, as has been reported by Warner[7] for biosynthetic polymers of high molecular weight.

Pronounced changes in the apparent *pK* values of the bases have also been observed. While in biosynthetic polymers of high molecular weight this could be due to hydrogen bonding in a macromolecular structure, in the smaller synthetic materials this is unlikely. Thus, the apparent *pK* of 2·32 found for guanosine-2′(3′) phosphate is shifted to 2·63 for polyguanylic acid (average chain-length 5·4 nucleotides), while that at 9·33 shifts to 10·76 for polyguanylic acid with an average chain-length of 5·4 units and to 11·20 for polyguanylic acid (average chain-length 12·5), using spectrophotometric titration to estimate apparent *pK* (Fig. 1).

Since the ionizable groups participate directly in the electron system giving rise to the absorption, any perturbation of the π-electron system of the purine or pyrimidine ring will have an effect on such groups. It is therefore considered that the hypochromic effect observed on formation of polynucleotides is essentially due to the interaction of π-electrons of adjacent rings (cf. refs. 8 and 9), with the formation of electron orbitals extending over more than one unit, orientated normal to the planes of the ring systems stacked in layers above each other, forming

essentially a new electronic species. While this interaction has an effect on the ionizable groups, it is clear that perturbation of these groups—by hydrogen bonding, or by ionization—will also have its effect on the total chromophoric system, without, however, breaking the π-bond interaction between the bases, which exists even at the dinucleotide-level and at all values of the *p*H. Variation in ionic strength, changing the macromolecular configuration and distribution of charge in the vicinity of the chromophore, will also have an effect on this interaction and hence on the ultra-violet absorption.

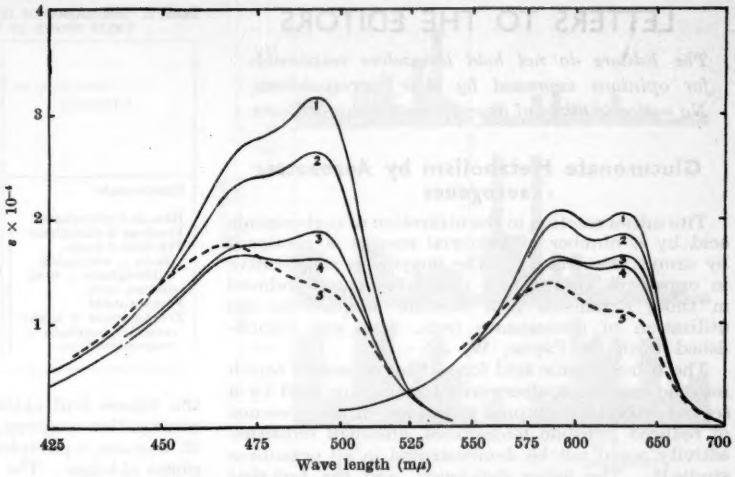

Fig. 2. Action of polynucleotides (3×10^{-5} *M*) on the absorption of acridine orange (3×10^{-5} *M*)—left; and toluidine blue (3×10^{-5} *M*)—right, in 0·01 *M* ammonium acetate at *p*H 6·8. 1, Dye alone; 2, 3, 4 and 5, with added polyuridylic acid, polyadenylic acid, polyguanylic acid and yeast ribonucleic acid, respectively

In view of the extensive work on the binding of various planar basic dyes and aminoacridines with nucleic acids, the effect of some low molecular weight synthetic polymers (average chain-length approximately 6) on the absorption spectra of rosaniline, toluidine blue and acridine orange was examined (Fig. 2). In all cases the effects due to the synthetic polymers were smaller than those observed with yeast nucleic acid. Since the linkages in the synthetic materials are mixed 2′–5′ and 3′–5′, the arrangement of phosphate groups along the backbone is not as uniform as in the natural material, so that while all sites may have been occupied, only where tracts of 2′–5′ or of 3′–5′ linkages occurred would any metachromasy result, giving rise effectively to 'dimeric' binding, rather than 'polymeric', using Lawley's[10] definition of the terms. Marked quenching of the fluorescence of acridine orange was also observed, particularly by polyguanylic acid and to a lesser extent by polyuridylic acid. Polyglycerophosphate[6] with an average chain-length of 12·1 glycerophosphate units was quite without effect on the absorption of these dyes or on the fluorescence of acridine orange,

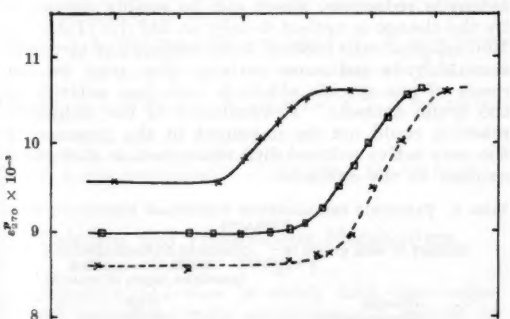

Fig. 1. Spectrophotometric titrations at 270 mμ of guanosine-2′(3′) phosphate —×—×—, polyguanylic acid (average chain-length 5·4) —□—□—, and polyguanylic acid (average chain-length 12·5) —×—×—

indicating the stereospecific requirements of the phosphate binding sites leading to induced metachromasy. That this induced metachromasy is a direct parallel to the similar effects observed in concentrated solutions of such dyes, and to the hypochromicity of polynucleotides, is further suggested by work which has shown that the forces operating between the rings of the neighbouring ions of dye aggregates have an equilibrium distance of 3–4 A.[11,12].

These three lines of evidence—the hyperchromic degradation of polymers, the corresponding hypochromic effect on the absorption of dyestuffs in combination with the polymer and the shift in apparent *pK* of the ionizable groups—point to a definite configuration for small polynucleotides and imply a restricted rotation about the internucleotide linkage even for dinucleotides. That the configuration favouring interplanar interaction may be of lower energy than other configurations has been shown by the effect of adenosine on the spectrum and fluorescence of riboflavin, particularly in flavin adenine dinucleotide[13].

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LETTERS TO THE EDITORS

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Glucuronate Metabolism by *Aerobacter aerogenes*

The initial reaction in the utilization of D-glucuronic acid by a number of bacterial species is catalysed by uronic isomerase[1-3]. The enzyme is constitutive in organisms that utilize glucuronate and induced in those organisms that become adapted to the utilization of glucuronate (refs. 2, 3 and unpublished work by Payne, W. J.).

The D-fructuronic acid formed by isomerase action may be converted afterwards to L-gulonic acid by a second enzyme, keturonic reductase, in the presence of reduced pyridine nucleotides, although reductase activity could not be demonstrated in all organisms studied[3]. The latter deficiency, and the fact that organisms adapted to uronate are not adapted to utilization of xylitol or the homologous aldo- or keto-pentoses expected from decarboxylation of gulonic acid, indicated that fructuronate might be metabolized by another pathway.

Table 1. Products of Anaerobic Glucuronate Metabolism in Whole Cells

Anaerobic metabolism by	Δ Glucuronate (μmoles)	Δ Hydrogen (μmoles)	Δ Carbon dioxide (μmoles)	Δ Volatile acid (μmoles)
Aerobically adapted cells	− 1·0	0·0	0·0	+ 2·58
Anaerobically adapted cells	− 1·0	+ 1·95	+ 1·70	+ 2·04

Products of the anaerobic metabolism of glucuronate by cells of *Aerobacter aerogenes* adapted to glucuronate utilization under aerobic and anaerobic conditions gave the stoichiometry shown in Table 1. These results suggested a cleavage to 3-carbon units according to the pathway:

glucuronate
⇅
fructuronate → (2 pyruvate) → 2 acetate + 2 formate → $2H_2 + 2CO_2$

The inability of aerobically adapted cells to produce gas is caused by the failure of such cells to form the hydrogenlyase system necessary for formation of hydrogen and carbon dioxide from formate. The formation of volatile acid without production of carbon dioxide by aerobically adapted cells excludes the possible decarboxylation of gulonic acid as an intermediate step in the pathway.

Confirmation of the cleavage to 3-carbon compounds was obtained by use of extracts of cells grown anaerobically on glucose or glucuronate and ground with alumina. Aldolase activity could be measured with 2,4-dinitrophenylhydrazine according to the method proposed for the measurement of the cleavage of hexose diphosphate[4], since the *bis*-2,4-dinitrophenylhydrazones formed from the products of fructuronate cleavage gave similar colour reactions. Prior phosphorylation to fructuronate-1-phosphate by adenosine triphosphate was necessary for the cleavage reaction (Table 2).

A comparison of the enzymatic activities of cells grown with glucose and with glucuronate shows that

Table 2. Comparison of the Enzymatic Activities in Extracts of Cells grown in Glucose and in Glucuronate

Additions	Enzyme(s) measured	C_4 compound metabolized (μmoles/hr./mgm. of protein)	
		Extract of cells grown in glucose	Extract of cells grown in glucuronate
Glucuronate	Uronic isomerase	0·00	18·60
Hexose diphosphate	Aldolase	7·24	2·86
Fructose 6-phosphate	Kinase + aldolase	0·00	0·00
Fructose 6-phosphate + adenosine triphosphate + magnesium ions		2·20	1·85
Fructuronate		0·00	0·00
Fructuronate + adenosine triphosphate + magnesium ions		0·09	0·05

the kinase and aldolase activities are the result of constitutive enzymes, probably non-specific reactions of fructose-6-phosphate kinase and hexose diphosphate aldolase. The specific activity of the induced uronic isomerase in the extracts is presented for comparison. The low activity of the kinase–aldolase system is apparently the rate-limiting reaction in the pathway, which thus accounts for the accumulation of fructuronate previously observed with dried cells[5]. Production of fructuronate-1-phosphate by the reverse reaction in the presence of dihydroxyacetone phosphate and tartronic semialdehyde can be measured with the cysteine–carbazole reaction[7]. No fructuronate was formed when dihydroxyacetone phosphate was replaced by dihydroxyacetone in the incubation mixture unless adenosine triphosphate and magnesium were also present.

The products of aldolase action, dihydroxyacetone phosphate and tartronic semialdehyde, are afterwards metabolized to acetate, hydrogen and carbon dioxide by extracts of anaerobically adapted cells. The dihydroxyacetone phosphate fragment is metabolized to pyruvate by normal glycolytic enzymes with the production of reduced diphosphopyridine nucleotide at the level of triose phosphate dehydrogenase. The reduced diphosphopyridine nucleotide is re-oxidized by hydrogen transfer to tartronic semialdehyde to yield, presumably, glyceric acid in the presence of another induced enzyme, tartronic semialdehyde reductase, which can be readily measured by the change in optical density at 340 mμ (Table 3). Non-adapted cells contain small amounts of tartronic semialdehyde reductase activity that may be the result of non-specific aldehyde reductase activity in the crude extracts. Reversibility of the reductase reaction could not be measured in the presence of the very active reduced diphosphopyridine nucleotide oxidase in the extracts.

Table 3. Tartronic Semialdehyde Reductase Activity of Cell Extracts

Extract of cells grown in:	Reduced diphosphopyridine nucleotide oxidized (μmole/hr./mgm. of protein)
Glucose	0·07
Glucuronate	0·57

Glyceric acid and 3-phosphoglyceric acid are metabolized to hydrogen and carbon dioxide by similar extracts. Preliminary results suggest that there is an initial phosphorylation by adenosine triphosphate prior to utilization of glycerate, but no glyceric acid kinase could be demonstrated in the crude extract by direct methods.

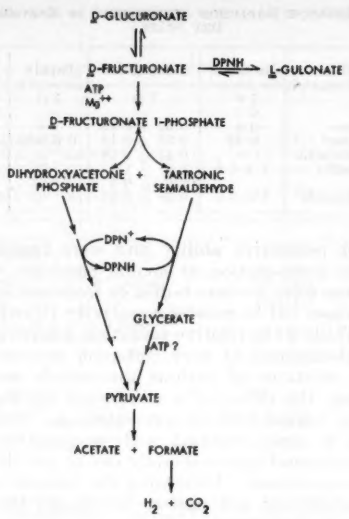

Fig. 1

Fig. 1 is a summary of the established reactions in the metabolism of glucuronate. The reactions leading to pyruvate probably represent the major pathway of glucuronate metabolism under aerobic as well as anaerobic conditions, since all the enzymes could also be demonstrated in extracts of aerobically grown cells.

Work is now in progress to isolate the enzymes from cells grown with glucose and with glucuronate, to determine the specificities of the induced and constitutive enzymes involved.

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Calcium and Phosphorus Metabolism after Surgery

CLINICALLY, the view is widely held that major surgical operations may encourage the growth of metastases in patients with certain types of cancer (stage III breast carcinoma, Wilm's tumour, bone and soft tissue sarcomas). It is possible that operative stress may favour the spread of tumours by affecting the adhesion between cells. In view of the known relation between lack of adhesiveness and low calcium content[1], an investigation of calcium and phosphorus metabolism in patients undergoing surgery has been undertaken.

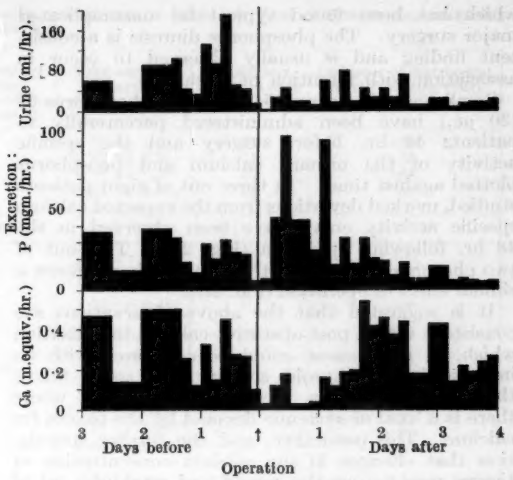

Fig. 1. The effect of a total hysterectomy (patient No. 246) on the urine, urinary phosphate and urinary calcium excretion rates

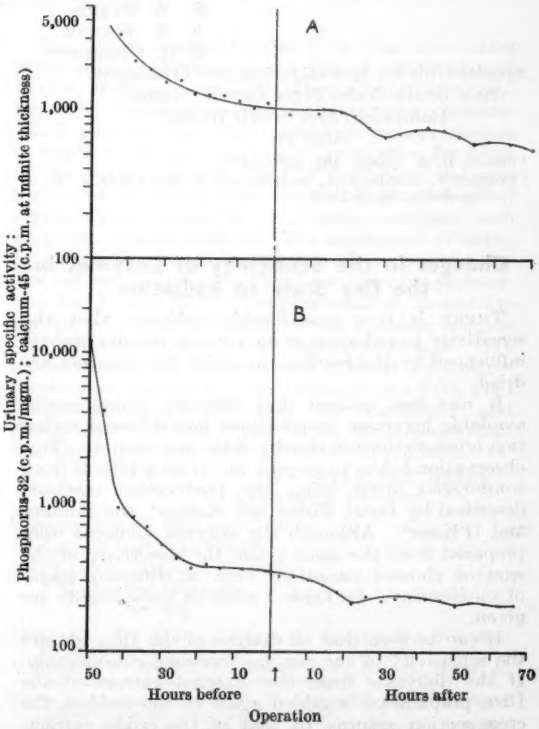

Fig. 2. *A*, The effect of a radical dissection of the inguinal lymph nodes (patient No. 611) on the specific activity of calcium-45 excreted in the urine (expressed as counts/min. of calcium oxalate at infinite thickness). *B*, The effect of an abdomino-perineal resection of the rectum (patient No. 486) on the specific activity of phosphorus-32 in the urine

Urinary excretion studies were carried out on 23 patients using four-hourly collection periods. Each collection has been analysed for calcium and inorganic phosphate and, in some cases, for total nitrogen, sodium, potassium, chloride and creatinine. Fig. 1 illustrates a calcium and phosphorus excretion pattern

which has been found typical for uncomplicated major surgery. The phosphorus diuresis is a consistent finding and is usually observed to occur in association with retention of calcium.

Small doses of calcium-45 (14 μc.) and phosphorus-32 (20 μc.) have been administered parenterally to patients 48 hr. before surgery and the specific activity of the urinary calcium and phosphorus plotted against time[2]. In three out of eight patients studied, marked deviations from the expected calcium specific activity curve have been observed in the 48 hr. following operation (Fig. 2*A*). Two out of two phosphorus specific activity curves have shown a similar effect of operation (Fig. 2*B*).

It is suggested that the above observations are consistent with a post-operative calcium mobilization which, in most cases, could be associated with an increase in parathyroid activity. It could follow that surgical trauma produces a condition where there is a local or systemic demand by the tissues for calcium. This possibility, and the further speculation that changes in the calcium concentration of tissues may favour the spread and establishment of metastases, are at present being investigated.

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Changes in the Sensitivity of Enzymes in the Dry State to Radiation

There is now considerable evidence that the sensitivity to radiation of enzymes in the dry state is influenced by the medium in which the enzymes are dried.

It was first noticed that different, commercially available invertase preparations had different radiation cross-sections in the dry state in a vacuum. This observation led us to prepare invertase solutions from commercial yeast using the purification methods described by Dieu[1], Fisher and Kohtes[2], and Sumner and O'Kane[3]. Although the enzyme solutions were prepared from the same yeast, the sensitivity of the enzyme showed variations even at different stages of purification. In Table 1 some of these results are given.

It can be seen that on dialysis of the Dieu extract the sensitivity of the enzyme increases considerably. If the dialysate from the dialysed extract of the Dieu preparation is added again to the residue, the cross-section returns to that of the crude extract. After free SH groups had been shown to be present in the yeast extract, cysteine and glutathione were tested for protective ability and were found to decrease the cross-section of several enzymes. Drying the enzyme from acetate buffer or from salt solutions in some cases led to greater sensitivity to radioactivity. In Table 2 the relative radiation sensitivities (for 4-MeV. deuterons) of four different enzymes dried down in solutions of various compounds are listed. In general, the effect of a compound on the radiosensitivity varied with its concentration. The results in Table 2 were obtained with a quantity of the added compound approximately one to ten times that of the enzyme used. Increasing the amount of compound added did not appear to change the values in Table 2 very much.

Table 1. Inactivation Cross-section (A.[2]) of Dry Yeast Invertase. 40 MeV. α-particles. Cross-section in yeast cell, 2,000 A.[2]

Purification method	Dieu	Sumner	Fisher
Crude extract	1,350 ± 50	1,400 ± 100	2,400 ± 100
Dialysed extract	2,500		2,300
Precipitation	3,200		1,900
Final product		2,550	3,800

Table 2. Relative Radiation Sensitivities of Enzymes in the Dry State

Additive	Invertase	Ribonuclease	Papain	Urease
Pure	1·0	1·0	1·0	1·0
Cysteine	0·5	—	—	0·5–0·7
Glutathione	0·5	0·52 ± 0·10	—	—
Yeast extract	0·45	0·52 ± 0·10	0·6–0·8	0·8
Ribonucleic acid	—	0·41 ± 0·07		
Acetate buffer	1·4–1·6	4·8 ± 1·4		
Sucrose		2·6 ± 0·5		
Sodium chloride	1·5–3·5	0·98 ± 0·21		

The conclusion to be drawn from these results is that the effect of ionizing radiation can either be increased or decreased. Reduction in radiation sensitivity of dry materials by added substances has recently been reported by Norman and Ginoza for catalase[4] and ribonucleic acid[5] and has been frequently observed in radiation studies on high polymers[6].

Further details will be reported elsewhere. This work was supported by a contract from the U.S. Atomic Energy Commission.

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Radioprotective Action of 5-Hydroxytryptamine

Tryptamine and its hydroxyl derivative are powerful radioprotective amines *in vivo*[1,2], but they also give rise to physiological changes. Bacq and Alexander[3] state that tryptamine is not a vasoconstrictor, but is nevertheless as good a radiation protector of mice as 5-hydroxytryptamine. However, tryptamine causes intense smooth muscle contraction, similar to its hydroxyl derivative[4,5]. While this pharmacological activity for tryptamine is much less, molecule for molecule[6], our studies indicate this also applies to its radioprotective properties in rats.

Both amines protect polymer irradiated in oxygenated solution *in vitro*[2], and Bacq and Alexander regard the protective action *in vivo* as one of competition for radicals (particularly $HO_2^\cdot$) from radiolysis of water. Others[4] have suggested that protection *in vivo* may be due to an 'oxygen effect'.

Table 1. EFFECTS OF 5-HYDROXYTRYPTAMINE AND 5-HYDROXYTRYPTAMINE ANTAGONISTS ON LETHALITY, LOSS OF WEIGHT AND DIARRHŒA IN IRRADIATED RATS

Group* (Treatment)	No. of animals: mean weight (gm.)	No. of survivors (30 days)	Mean survival (days)	Weight loss, initial 10 days	Incidence of diarrhœa at fourth day (per cent)
Experiment 1†					
Controls (saline)	15 (181)	0	8·07 (± 4·69)	35	100
5HT ($0·5 \times 10^{-5}$ mole)	15 (180)	9	21·40 (± 9·93)	11	13
LSD ($0·6 \times 10^{-7}$ mole)	15 (189)	0	9·93 (± 3·83)	48	64
LSD ($0·6 \times 10^{-7}$ mole) + 5HT ($0·5 \times 10^{-5}$ mole)	15 (178)	1	11·33 (± 6·68)	14	50
Experiment 2					
Controls (saline)	10 (145)	0	7·10 (± 2·03)	—	100
5HT ($0·5 \times 10^{-5}$ mole)	10 (145)	9	22·90 (± 6·17)	17	0
BAS-phenol ($1·7 \times 10^{-5}$ mole)	10 (148)	0	5·90 (± 2·65)	—	100
BAS-phenol ($1·7 \times 10^{-5}$ mole) + 5HT ($0·5 \times 10^{-5}$ mole)	10 (151)	0	7·10 (± 3·48)	—	100
BAS-phenol ($0·3 \times 10^{-5}$ mole) + 5HT ($0·5 \times 10^{-5}$ mole)	10 (146)	0	12·30 (± 1·97)	17	0
Experiment 3					
Controls (saline)	10 (149)	0	5·10 (± 2·58)	—	100
5HT ($0·5 \times 10^{-5}$ mole)	10 (149)	4	20·70 (± 9·12)	30	10
BOL 148 (3×10^{-7} mole)	10 (150)	0	6·10 (± 2·38)	—	30
BOL 148 (3×10^{-7} mole) + 5HT ($0·5 \times 10^{-5}$ mole)	10 (153)	0	8·80 (± 3·40)	—	71

* All injections given intraperitoneally; 5-hydroxytryptamine 5 min. before irradiation. For *d*-lysergic acid diethylamide, 1-benzyl-2-methyl-3-(2 aminoethyl) 5 methoxy indole hydrochloride (BAS-phenol) and BOL 148, single injections given 5 min. before irradiation, or 10 min. before irradiation were followed by 5-hydroxytryptamine.

† In experiments 1 and 2, Canberra Black stock rats were used in proportions of 2 males to 1 female for each group. In experiment 3 Wistar hooded female rats were used. All animals received 1,000 r. whole-body irradiation.

We have investigated the effect of pretreating rats with antagonists and specific anti-metabolites, preceding administration of 5-hydroxytryptamine and tryptamine, and its effect on acute lethality from total-body irradiation (1,000 r. X-rays). Results of some of these experiments are set out in Table 1, for the 5-hydroxytryptamine anti-metabolites, *d*-lysergic acid diethylamide (LSD), its brominated-derivative (BOL 148), and the anti-serotonin, 1-benzyl-2,5-dimethyl serotonin (BAS phenol)[6]. Acute lethality was assessed for a 30-day period following irradiation, as in previous experiments[7]. The loss of weight and incidence of diarrhœa in survivors was also charted.

Antagonists and anti-metabolites of 5-hydroxytryptamine alone had no significant protective action, but inhibited that of 5-hydroxytryptamine and tryptamine. Anti-histamines failed to influence the protective action of 5-hydroxytryptamine but the radioprotective action of histamine[8] was inhibited.

Atropine and dibenzyline, which respectively block two types of tryptamine receptors[9], in doses of 0·25 mgm. failed to influence the protective action of 5-hydroxytryptamine.

Tranquillization of rats with reserpine (20 mgm. per kgm.), 18 hr. before irradiation, did not influence lethality significantly. Given 5–10 min. before irradiation, a slight protection resulted which could be increased by pretreatment with iproniazid (100 mgm./kgm.) given 12 hr. before reserpine. However, administration of 5-hydroxytryptamine 5 min. before irradiation to reserpinized rats resulted in a radioprotective effect, comparable to 5-hydroxytryptamine alone in similar doses. Reserpine exerts a non-specific antagonism to 5-hydroxytryptamine and other amines in smooth-muscle preparations[10], and besides releasing and depleting these amines by a change from bound to free form, apparently reduces their capacity to react with cell receptors. An anti-metabolite (for example, 1-benzyl-2,5-dimethyl serotonin) is pictured as acting by excluding a structurally related metabolite (5-hydroxytryptamine) from combination with its normal specific reactant (5-hydroxytryptamine receptor)[11].

The results obtained point to a close correlation between the radioprotective action of certain amines *in vivo*, and their respective pharmacological actions. However, the narrow range of tissue oxygen tension, which governs the oxygen effect in radioprotection *in vivo*[12], seems an inadequate explanation for some of the results obtained, and in particular, the protection which results from the endogenous release of 5-hydroxytryptamine by combining reserpine with an amine oxidase inhibitor. The conception of radioprotection *in vivo* as largely one of competition for free radicals, also fails to afford a convincing explanation for the specificity of antimetabolites, in modifying the protective action of certain aromatic amines.

A full report will be published elsewhere. We thank Sandoz, Ltd., for liberal gifts of 5-hydroxytryptamine, lysergic acid diethylamide and BOL 148; Roche Products Pty., Ltd., for marsilid; and Merck and Co., Ltd., New York, for 1-benzyl-2,5-dimethyl serotonin, used in these experiments.

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Liberation of Invertase from Disintegrated Yeast Cells

Myrbäck[1,2] found that if baker's yeast was treated with ethyl acetate for 20 hr. at room temperature and then thoroughly washed with water on the centrifuge a large proportion of its invertase activity remained in the insoluble fraction even when this was stored for several months at room temperature. It has long been known[3] that only a small fraction of the total invertase can be removed from yeast cells by simple extraction procedures, some form of autolysis being needed to liberate the remainder. Myrbäck suggested that treatment with ethyl acetate removes from the cell the enzymes responsible for the autolytic release of the invertase, which therefore remains indefinitely in combination with insoluble cell structures.

We have confirmed the effect of ethyl acetate treatment, but have obtained additional evidence which indicates, contrary to Myrbäck's view, that yeast invertase does not occur in an insoluble form.

In our experiments we used baker's yeast from a factory at Libán, Czechoslovakia. 150 gm. was kneaded with 15 ml. redistilled ethyl acetate; it liquefied, and was then shaken for 20 hr. at room temperature. After dilution to 1,500 ml. with distilled water the insoluble fraction was separated and washed repeatedly on the centrifuge, the final wash being colourless and virtually devoid of invertase activity. The precipitate was suspended in water to a total volume of 150 ml., and when plated on wort-agar showed no sign of living cells. It was preserved at room temperature with chloroform.

The total invertase content of each batch of yeast was assumed to be the sum of the activities of the final ethyl acetate-treated suspension and of the first supernatant, measured by a polarimetric method. All results are expressed in units per gm. original pressed yeast, one unit being that quantity of enzyme which inverts 1 mgm. sucrose/min. from a 5 per cent solution at *p*H 4·7 (0·02 *M* sodium acetate buffer) at room temperature (20–22° C.).

Experiments were made with suspensions freshly prepared, or at most 7 days old. During this period not more than 5 per cent of the invertase activity passed into the suspending fluid. Samples were centrifuged and the precipitates crushed in the Hughes press[4]. For example, 10 ml. of a suspension was centrifuged (1,000*g*) on the day it was prepared and a known fraction of the precipitate transferred to the Hughes press, crushed at −30° C., and washed off the block and re-suspended with water so that 1 ml. corresponded to 0·5 gm. of original yeast. On centrifugation for 1 hr. at 35,000*g* a slightly opalescent supernatant was obtained. Its invertase activity was 57 units, compared with 65 units for the suspension before crushing and an estimate of 72 units in the original yeast.

This result suggests that the invertase in the intact yeast cell is enclosed by membranes which are not permeable to it, and which are not sufficiently damaged by ethyl acetate treatment to allow it to escape. It is conceivable that one of the membranes concerned is the glucan layer of the cell wall[5]. Treatment with crop juice of *Helix pomatia*[6], which is known to attack this glucan[7], at a final dilution of 1 : 10, liberated practically all the invertase (125 out of 130 units) from a sample of ethyl acetate-treated material in 8 hr. at 20° C. It has been suggested that invertase must lie near the surface of the yeast cell[3], and so it is possible that it lies between the glucan layer and a protein-containing layer[5]. This might explain the liberation of invertase by the action of papain[1].

It is unlikely that invertase is solubilized by autolytic processes during the ethyl acetate treatment, because the crushing of washed samples of living baker's yeast liberates a large proportion of the invertase in a water-soluble form. Further, on treatment with 0·1 volume of undiluted snail crop juice at room temperature some 50 per cent of the invertase of a sample of living yeast was liberated in 10 hr., while at least 90 per cent of the cells remained viable.

The preparations treated with ethyl acetate retain the outward shape of yeast cells but have obviously lost a great deal of their contents. After crushing, many of the cells show gross destruction, and, on prolonged treatment with snail digestive juice, holes appear in the cell walls. However, it would seem that often quite minor damage is sufficient to set the invertase free. Myrbäck's ethyl acetate-treated preparations might therefore provide a useful and sensitive system for the investigation of the nature of the yeast cell wall.

Two of us (E. E. B. and J. S. D. B.) wish to thank the Czechoslovak Academy of Sciences and Academician I. Málek, director of the Institute, for most generous hospitality which made our participation in this work possible.

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Critical Effect of Oxygen Tension on Rate of Growth of Animal Cells in Continuous Suspended Culture

Its relevance to current animal virus and cell culture work prompts us to report the feasibility of and requirements for continuous culture of cells in suspension; full details will be given elsewhere.

Medium was pumped at a known rate from a reservoir to a culture vessel kept at 37° C. (20-l. 'Pyrex' aspirators), which overflowed at a constant level into a cooled receiver and was harvested once weekly. Culture vessel and receiver were gassed with mixed carbon dioxide, oxygen and nitrogen and magnetically stirred. Mechanical reliability was essential, as small breakdowns were rapidly lethal. The medium, a modified Earle's saline plus lactalbumen hydrolysate, amino-acids, yeast extract, vitamins, horse and calf serum, contained most components at their highest non-toxic level; these levels are probably not vital for continuous culture except for glucose (6–8 gm./l.). The limiting cell-density was probably not reached, but growth was very rapid under optimal conditions (defined below). Varying the gas-phase carbon dioxide and including bicarbonate kept the *p*H neutral; a transformed em-

bryo rabbit kidney cell line[1] was used. The system was not self-balancing (not a 'chemostat'), as limitation of medium did not much restrict growth without inducing a sometimes irreversible lag. Since 'steady state' therefore rarely occurred and since synchrony was also possible, growth-rates were not known precisely; they were recorded as 'percentage increase/24 hr.', based on the culture vessel content of a given day. Cells were counted and medium flow-rate, gas-phase carbon dioxide and oxygen levels adjusted daily to control *p*H, cell density and growth-rate. Medium changes were not needed, flow-rate being generally matched with growth-rate; carbon dioxide was 2–5 per cent and oxygen was 5–24 per cent (v/v), cell-density was 5–20 × 10^5 ml., and *p*H was roughly 6·9–7·2.

This system produced in four months continuous medium flow an average of 10^9 (2 gm. wet weight) cells/day in 1 l. of medium from a constant culture volume of 1·5 l. (Fig. 1). The mean doubling time was 25 hr., and sometimes 16 hr. or less. Continuous growth was more efficient and less troublesome than batch culture, in which the narrow optimal ranges of animal cells were soon exceeded. The cells were used for agar-suspension plaque assay[2] and suspension growth of polioviruses, making 10^{11} to 10^{12} plaque-forming units per week.

Unexpectedly, cell growth-rate was very dependent on oxygen levels. The gas mixtures bathing tissue cultures have hitherto had little attention, air (20 per cent v/v oxygen) or 5 per cent carbon dioxide-in-air (19 per cent oxygen) generally sufficing. We find that 20 per cent oxygen and above is relatively inhibitory, and once during a steady state a small drop (from 19 to 17 per cent oxygen) increased the growth-rate by 50 per cent. On another similar occasion, a small increase (from 22 to 24 per cent) halved the growth-rate, while in other experiments 25–30 per cent oxygen was rapidly cytocidal. Since the important factor is the liquid-phase oxygen level or equivalent redox potential, the gas-phase oxygen level for optimal growth at high cell density depends on rates of agitation, oxygen exchange across the surface and oxygen uptake/cell, surface area and depth of culture and cell density. Thus apparent doubling times were 24 hr. or less with oxygen-levels from 14 to 22 per cent (other conditions being constant), but cell densities allowing such optimal growth were always higher at higher oxygen-levels (Table 1). Growth-rates and cell densities were cyclic (Fig. 1). Starting with slight excess of oxygen, a slight rise in cell density decreased liquid-phase oxygen-levels, and growth-rate rose. Cell density also rose, presumably passing through optimal to hypoxic levels of oxygen, when the *p*H fell and growth almost stopped; this resembled a lag, as optimal conditions did not at once restore growth-rate.

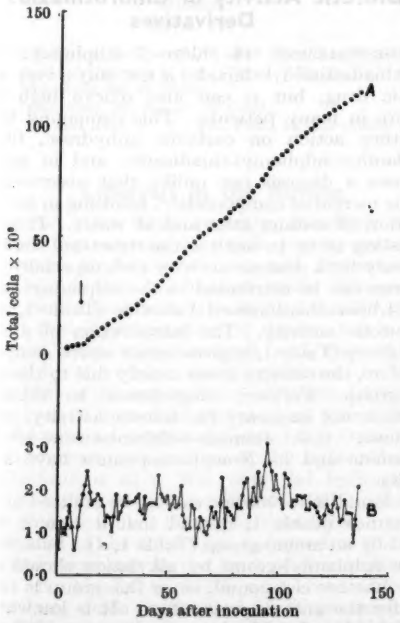

Fig. 1. Continuous growth of animal cells in suspension: *A*, cumulative production; *B*, culture vessel content. The medium was not varied and *p*H was 6·9–7·2; oxygen levels were often varied. Arrows indicate time when continuous flow started

Table 1. Mean Gas-phase Oxygen and Culture-Vessel Cell Densities (see Fig. 1) when the Cell Increase/24 hr. exceeded 87 per cent (Probable Mean Doubling Times of 24 hr. or Less)

Percentage oxygen	14	16	16·5	17	18	20	22
Cells/ml. × 10^5	7·8	8·3	10·0	11·3	12·6	13·4	18·0

We conclude that liquid-phase oxygen-levels for fastest growth of these cells is much less than air (and even 14 per cent oxygen) equilibrium values; this has interesting implications for the usual stationary cultures.

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Effect of Oxytocin Administration on Respiration of Lactating Mammary Gland Tissues in Rats

The participation of the hypothalamus and the posterior lobe of the pituitary in milk ejection is well known. On the other hand, the importance of the suckling stimulus in maintaining the secretion of milk[1], suggested that the hypothalamus and the posterior lobe of the pituitary played some part in controlling the secretion of anterior pituitary galactopoietic hormones.

Recently, Benson and Folley[2] reported that the administration of oxytocin to a lactating rat retarded the mammary involution which occurred after weaning, and suggested the possible part which oxytocin plays in the release of prolactin and other lactogenic and galactopoietic hormones from the anterior pituitary gland. Since Benson and Folley obtained their results by a histological method and discussed the problem from this point of view, it is of interest to use a biochemical method for comparison. Therefore, as an indicator of the activity of the gland, the respiration and rate of production of lactic acid by the tissue slices were employed. The following experiments were carried out:

Table 1. Effects of Oxytocin Administration on Respiration and Lactic Acid Production of Rat Mammary Gland Tissues

Group	Respiratory quotient	$Q(O_2)$ (μl./mgm. dry wt. of tissue/hr.	Lactic acid produced (μgm./mgm. dry wt. of tissue/hr.)
Oxytocin 1·0 I.U. treated	(*a*) 0·92±0·04* (5)	7·15±3·66 (5)	6·71±4·06 (5)
Oxytocin 2·0 I.U. treated	(*b*) 0·92±0·05 (4)	7·08±3·03 (4)	4·97±2·57 (3)
Intact weaning control	(*c*) 0·94±0·03 (6)	6·11±1·17 (6)	5·58±2·26 (6)
Normal control	(*d*) 1·32±0·09 (4)	14·81±3·46 (4)	2·41±0·34 (3)

Figures in parenthesis represent the number of animals. * 95 per cent fiducial limits. *a* and *b* are not significantly different from *c* ($P < 0·01$); *a*, *b* and *c* are significantly different from *d* ($P > 0·2$).

Nineteen Wistar strain female rats in the first lactation, weighing 160–190 gm., were used. Litters were reduced to six on the first day of lactation, three of each sex being kept whenever possible. They were weaned on the twelfth day of lactation. Oxytocin (1·0 and 2·0 I.U. 'Pituitan': Dainippon Zoki Lab., Osaka) diluted in 0·5 ml. of distilled water, was injected intraperitoneally to nine mothers three times a day, beginning on the afternoon of the weaning day. 3 days after weaning (fifteenth day of lactation and 30 min. after the last injection), the animals were killed by decapitation. Six rats kept intact for 3 days after weaning, which occurred on the twelfth day of lactation (intact weaning control), and four rats on the fifteenth day of lactation (normal control), were used as controls.

The respiratory quotient and oxygen consumption of tissue slices from the mammary glands of these animals were measured manometrically with special flasks[3]. Incubations were carried out in a Krebs–Ringer phosphate solution (*p*H 7·4) containing 0·3 per cent glucose, with a 100 per cent oxygen gas phase—for 2 hr. at 37° C. The amount of lactic acid in the medium was determined chemically[4] after the incubation, and was expressed in terms of μgm./hr./mgm. final dry weight of the slices.

A steep decrease in the respiratory quotient and $-Q(O_2)$ value resulted from the weaning, the normal control tissue slices retaining high values. The rate of production of lactic acid increased after weaning, but remained low in the normal controls. These changes were not affected by oxytocin (Table 1). Vaginal cornification was observed within 2 or 3 days after weaning in both the oxytocin-treated and intact weaning control groups.

During the experimental period (3 days), the alveoli of the mammary glands of both the oxytocin-treated groups and the weaning control group were abundantly filled with milk, and histologically there was no evidence of involution. This observation was consistent with that of Benson and Folley[2] for the mammary gland 6 days after weaning.

The diminution of the respiratory quotient and the recurrence of œstrus may indicate the ineffectiveness of oxytocin on the galactopoiesis of mammary glands and on the maintenance of luteal activity in the ovaries. (This activity of oxytocin was reported by Desclin[5].) Nevertheless, we must take into consideration the results of Cross and Silver[6], who pointed out the importance of engorgement as a cause of the involution taking place after weaning. This suggests that, even if oxytocin has a galactopoietic effect, engorgement may overcome it.

In order to determine the essential role of oxytocin in galactopoiesis, the effects of engorgement of the mammary gland must be eliminated. The experiment, furthermore, must be carried out under conditions which suppress the suckling stimuli completely, since these stimuli are considered to reach the hypothalamus and to cause not only the release of oxytocin from the posterior lobe of pituitary, but also that of the galactopoietic hormones from the anterior lobe. Studies on this problem are now in progress.

After this communication had been sent to *Nature*, we were informed by Dr. A. T. Cowie, of the National Institute for Research in Dairying, Reading, England, that similar results had been obtained independently by Dr. M. L. McNaught[7]. She reported that, in rats, no significant differences in the respiratory activity *in vitro* of mammary gland slices were found between a group receiving 1 I.U. of oxytocin during the 12 hr. after removal of the litter, and a group receiving no oxytocin. She also discussed the effect of accumulation of milk.

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Diuretic Activity of Chlorothiazide Derivatives

Chlorothiazide (6-chloro-7-sulphamyl-1,2,4-benzothiadiazine-1,1-dioxide) is not only a very active diuretic drug, but it can also relieve high blood pressure in many patients. This compound has an inhibitory action on carbonic anhydrase, like N-acetylamino-sulphamyl-thiadiazole, and in addition it causes a diuresis not unlike that observed with organic mercurial compounds[1,2], resulting in increased excretion of sodium salts and of water. It seemed interesting to us to analyse the structural conditions necessary for a diuretic activity and, especially, what influence can be attributed to the sulphamyl-group.

1,2,4-benzothiadiazine-1,1-dioxide (Table 1, *a*) has no diuretic activity. The introduction of a sulphamyl-group (Table 1, *b*) gives barely active compound. Therefore, the activity is not mainly due to the sulphamyl-group. Further, ring-closure to thiadiazin-dioxide is not necessary for diuretic activity, since it is known[3] that 4-amino-6-chlorobenzene-1,3-disulphonamide and its N-acyl-compounds have a high activity.

We found that chlorine cannot be omitted in these compounds (Table 1, *c*), and that it cannot be replaced by an amino-group (Table 1, *d*). Substitution of the sulphamyl-group by alkylation should result in an inactive compound, since this group is responsible for the anti-enzymic effect. It is known[4] that N-alkyl-chlorothiazides have no diuretic activity, but to our great surprise we found a highly active and considerably less toxic compound in 4-amino-6-

Table 1

	Compound	Melting point (deg. C.)	Activity*
a	1,2,4-benzothiadiazine-1,1-dioxide	219–220	1·46
b	7-sulphamyl-1,2,4-benzothiadiazine-1,1-dioxide	319–320	1·34
c	4-amino-benzene-1,3-disulphonamide	232	1·24
d	4,6-diamino-benzene-1,3-disulphonamide	253	0·62
e	4-amino-6-chloro-benzene-1,3-disulphonmethylamide	182	2·48
f	4-amino-6-chloro-benzene-1,3-disulphonallylamide	132	1·64
g	4-amino-6-chloro-benzene-1,3-disulphonbutylamide	97	1·79
h	4-amino-6-chloro-benzene-1,3-disulphondimethylamide	184	1·99
i	4-amino-6-chloro-benzene-1,3-disulphonmorpholinamide	158	0·82
j	4-amino-6-chloro-benzene-1,3-disulphon*cyclo*hexylamide	189	1·19

* Activity: $\frac{\text{Urinary excretion of treated animals}}{\text{Urinary excretion of untreated animals}}$ (ref. 5)

chloro-benzene-1,3-disulphonmethylamide (Table 1, *e*). Therefore, a free sulphonamide group is definitely not necessary for diuretic activity.

Activity decreases rapidly with increasing molecular weight of the alkyl-group (Table 1, *f* and *g*). The dimethyl compound (Table 1, *k*) still has activity and the morpholine compound slight activity, but the cyclohexyl-compound (Table 1, *i* and *j*) is inactive.

Further particulars, especially the pharmacological properties of the compound of Table 1, *e* will be described elsewhere.

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Lipolysis in the Rumen

Reiser[1], and more recently Shorland *et al.*[2], reported experiments in which rumen contents of sheep were incubated *in vitro* with linseed oil and with oleic, linoleic and linolenic acids. These experiments, and others using the living animal[3–5], demonstrated that hydrogenation of double bonds of unsaturated fatty acids occurred and that this was effected by the rumen micro-organisms.

We have done experiments in which triglycerides in the form of linseed oil and tung oil were incubated with the rumen contents of sheep (1·0 gm. per 100 ml. rumen contents) in a manner similar to that described by Shorland *et al.*[2]. Not only did hydrogenation occur as indicated by a considerable fall in the iodine value of the lipid, but it was also found that more than 75 per cent of the total lipid recovered at the end of the incubation was in the form of free higher fatty acids. In 'blanks' to which no oil was added, free higher fatty acids represented 50–60 per cent of the total lipid present. Rumen contents obtained from animals fed on rations containing hay and either potato starch and mixed concentrates (including fish meal) or flaked maize, maize meal, groundnut meal and oats gave similar results.

That the lipolysis is the result of enzyme action was demonstrated by incubating linseed oil (iodine value, 181·3) with rumen contents obtained from a fistulated sheep 4 hr. after the last feed of hay and mixed concentrates and with the same rumen contents which had been previously heated in a boiling water-bath. The results of one such experiment are given in Table 1. After allowing for the difference between the amounts of free fatty acids in flasks 2 and 4, it is calculated that about 60 per cent of the esterified fatty acid residues were liberated from the oil in flask 2. No lipolysis was observed in flask 4, the slight difference between the amounts of fatty acids recovered from flasks 3 and 4 being due to the traces of free acid originally present in the linseed oil. Noteworthy is the low iodine value of the fatty acids derived from rumen contents alone; calculation gives the iodine value of the acids resulting from lipolysis in flask 2 as 121·4, which represents a decrease of about 70 units compared with the iodine value of the acids present initially in glyceride combination.

Table 1. Amounts and Iodine Values of Free Higher Fatty Acids found after Incubating Sheep Rumen Contents, with and without the Addition of Linseed Oil, at 37° C. for 24 hr. (Each flask contained 100 ml. rumen contents)

Flask	Treatment before incubation	Addition	Free fatty acids	
			Weight (mgm.)	Iodine value
1	None	None	245	22·8
2	None	Linseed oil (1·00 gm.)	859	97·4
3	Heated at 90° C. for 1 hr.	None	236	31·6
4	Heated at 90° C. for 1 hr.	Linseed oil (1·00 gm.)	268	44·7

Extensive lipolysis of ingested glycerides in the rumen of the intact animal was found on examination of the contents of the alimentary tract of a sheep which had been fed for several months on a diet consisting largely of hay, linseed meal and maize to which 40 gm. of linseed oil were added daily. At slaughter, 7 hr. after the last feed, 80–90 per cent of the lipid in the rumen, abomasum and upper part of the small intestine was in the form of free higher fatty acids of iodine value about 70. In the lower part of the small intestine the free fatty acids comprised 68 per cent of the total lipids and had an iodine value of 48.

Saliva is one of the main constituents of the liquid phase of rumen contents, but no lipolytic activity towards linseed oil could be demonstrated in samples of adult sheep saliva which were made available to us by our colleague Dr. R. N. B. Kay. It is therefore presumed that micro-organisms are responsible for the production of a lipase in the rumen; in this connexion it is of interest to note that Johns[4] has already shown that glycerol is fermented slowly in the sheep's rumen to yield propionic acid.

Our preliminary observations indicate that, in the ruminant, dietary triglycerides reach the small intestine largely in the form of free fatty acids, of which the unsaturated components have been modified by hydrogenation. This is in marked contrast to the digestion of lipids in adult monogastric animals in which little or no lipolysis occurs before triglycerides of long-chain fatty acids reach the intestine

Further studies, both biochemical and bacteriological, on the fate of ingested lipids in the alimentary tract of ruminant animals are in progress.

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Metabolism of 16-Oxoœstrone by Human Liver Slices *in vitro*

Layne and Marrian[1] recently reported the isolation of 16β-hydroxyœstrone from the urine of pregnant women, and Brown, Fishman and Gallagher[2] detected the same compound by reverse isotope dilution in the urine of a human subject after the administration of œstradiol-17β-16[14]-C. In the course of our own studies on the metabolism of œstrogens *in vitro*, 16β-hydroxyœstrone has been found after incubation of 16-oxoœstrone with normal human liver slices. In addition, five other phenolic steroids have been identified as metabolites of 16-oxoœstrone.

In a typical experiment, 200 mgm. of liver slices were incubated with 100 μgm. of 16-oxoœstrone in 5 ml. Krebs phosphate saline for 60 min. at 37° C. The incubation medium and the tissue were extracted twice with equal volumes of an ether-chloroform mixture (3 : 1 v/v). In order to separate 16-oxoœstrone from the higher polar transformation products, the extracts were subjected to paper chromatography in the system benzene/methanol/water (100 : 55 : 45). The material more polar than 16-oxoœstrone was eluted and resubjected to chromatography in the system formamide/chloroform. After spraying the paper with Folin and Ciocalteu's reagent[3] eight substances (I–VIII) were detected, six of which had the same mobility and showed the same absorption curves in the Kober reaction as pure œstriol (II), 16-epi-œstriol (IV), 17-epi-œstriol (V), 16β-hydroxyœstrone (VI), 16-oxo-œstradiol-17β (VII) and 16α-hydroxyœstrone (VIII). For further identification, the metabolites were coupled with fast black salt *K* to make azo derivatives, followed by paper chromatography in the system toluene/petroleum ether/ethanol/water (200 : 100 : 30 : 70)[4]. With substances II and IV–VIII well-defined spots were formed, identical in all ways with spots produced by parallel runs of (R_F values in brackets) œstriol (0·07), 16-epi-œstriol (0·46), 17-epi-œstriol (0·32), 16β-hydroxyœstrone (0·56), 16-oxoœstradiol-17β (0·77) and 16α-hydroxyœstrone (0·60), respectively. In the sulphuric acid/water reaction[5] the absorption spectra of substances II, IV, V, VII and VIII were identical with those of (maxima in brackets) œstriol (282 ; 458 mμ), 16-epi-œstriol (290 ; 457 mμ), 17-epi-œstriol (286 ; 456 mμ), 16-oxoœstradiol-17β (272 ; 503 mμ) and 16α-hydroxyœstrone (270 ; 507 mμ) respectively. When substance VI was reduced with sodium borohydride, a compound was formed which was in every respect indistinguishable from 16-epi-œstriol. Since on reduction of authentic 16β-hydroxyœstrone with sodium borohydride only 16-epi-œstriol is formed while 16-oxoœstradiol-17β is reduced to 16-epi-œstrol as well as œstriol, it is concluded that substance VI is identical with 16β-hydroxyœstrone.

The quantitative examination of the extracts revealed that 16-oxoœstrone was metabolized very rapidly by human liver slices. The main metabolites were 16-oxoœstradiol-17β and 16β-hydroxyœstrone, whereas œstriol and 16-epi-œstriol were formed in smaller amounts. 16α-Hydroxyœstrone and 17-epi-œstriol were minor metabolites. It is interesting that we failed to detect any of the 16- or 17-hydroxy ring *D* ketols after incubation of œstriol, 16-epi-œstriol or 17-epi-œstriol with human liver. These findings and the experiments reported here support the view that the hydroxy ring *D* ketols are mainly derived either from direct hydroxylation[6] or, less probably, from oxidation and subsequent reduction[7] of œstrone rather than from oxidation of the corresponding triols. This concept, however, does not exclude the possibility that, to a small extent (less than 1 per cent), the triols can be oxidized to ring *D* ketols, as has recently be shown by Levitz, Spitzer and Twombly[8].

Full details will be published elsewhere. This investigation was supported in part by research grants from the Government of Nordrhein-Westfalen.

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Pregnanediol in the Urine of the Ewe

The establishment of the relationship between progesterone and 5β-pregnane-3α : 20α-diol by Venning[1] was followed by a number of reports of the isolation of pregnanediol from the urine of other species.

Marker[2] reported that considerable quantities of pregnanediols were present in the urine of pregnant cows, bulls and steers, but Stevenson[3] and Hill[4] were unable to substantiate these findings.

Aparici[5] claimed to have measured large quantities of pregnanediol in the urine of pregnant cows but he did not isolate and characterize the material which he measured. In a recent comprehensive study of the lipid fraction of pregnant cow urine, Klyne and Wright[6] failed to identify any pregnanediol, but in a similar study of pregnant goat urine[7] they found a pregnanediol concentration of 2 mgm. per litre.

As part of an investigation on progesterone metabolism in the ewe, 20 l. of pooled urine from ten pregnant ewes in the fourth month of pregnancy were

hydrolysed, extracted by the usual methods, and chromatographed on alumina.

The fraction corresponding to 5β-pregnane 3α : 20α-diol, yielded, after recrystallization from ethanol–water, 35 mgm. of white crystals which melted at 234–236° C. and gave no depression when a mixed melting point was determined with authentic 5β-pregnane 3α : 20α-diol. The infra-red spectra of this material matched that of authentic pregnanediol.

The work was repeated on 10 l. of pregnancy urine collected from other ewes a year later and a similar result was obtained. 10 l. of urine from ancestrous ewes was investigated by similar methods and no trace of pregnanediol was found.

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Ribosyl Transfer between Ribose Nucleotides in the Rat

IN the course of studies on alterations in the rate of catabolism of nucleic acids induced by radiation after total body exposure of rats, evidence has been obtained of the existence of an exchange between the ribosyl residues of purines and pyrimidines and urinary imidazole acetic riboside. The latter riboside has served as a measure of the isotope concentration in the ribose pool of the rat. Hiatt *et al.*[1] have reported recently an application of this 'metabolic trap' to the study of mechanisms by which glucose is metabolized *in vivo*, particularly with respect to the contribution of the glucose-6-phosphate oxidative shunt to the metabolism of glucose. The use of imidazole acetic riboside as a device for trapping ribosyl residues has been made possible by the findings of Tabor and his collaborators[2,3], who have demonstrated that imidazole acetic riboside is one of the major urinary excretion products of imidazole acetic acid.

In a typical experiment, a rat weighing 194 gm. was injected intraperitoneally with 2 μc. of cytidylic acid-^{14}C (uniformly labelled) equivalent to 8·5 × 10^5 c.p.m. and 8 mgm. of imidazole acetic acid. Urine was collected for 20 hr. thereafter; the rat was killed at the end of the 20-hr. period.

The ribonucleic acid fraction of the liver was isolated as described by Paine *et al.*[4]. The (free) nucleotide fraction soluble in acid was adsorbed on activated charcoal ('Norite' *A*) from the supernatant resulting from treatment with perchloric acid and was then eluted according to the procedure of Cabib *et al.*[5]. The nucleotide polyphosphates thus obtained were converted to their corresponding monophosphates which, in turn, were separated by paper chromatography[6]. The ribonucleic acid fraction was hydrolysed by Schmidt and Thannhauser's method[7] and the resulting nucleotides separated and isolated by Hurlbert and Potter's procedure[8].

The isolation of imidazole acetic acid from urine was accomplished as follows: (*a*) Removal of substances insoluble in 66 per cent aqueous methanol (v/v); (*b*) placing the methanol-soluble fraction on a column of 'Amberlite 120'(H^+), removal of glucose and pentoses by washing the column with water, and elution of the riboside with 2 *M* ammonium hydroxide; (*c*) final purification of the effluent fraction containing riboside by means of paper chromatography in two different solvent systems[2]. Imidazole acetic riboside was eluted from the paper strips with methanol. The methanol was distilled off and the riboside concentration was determined quantitatively in an aqueous solution of the residue in terms of periodate consumption[9]. The aqueous washings of the 'Amberlite 120' column were passed through a column of 'Amberlite *IR* 400' (acetate form, 16–50 mesh). Glucose and pentoses were not retained by this column and were isolated from the effluent solution by paper chromatography[10]. After treatment of the paper strips with aniline phthalate, appropriate areas of the chromatograms were eluted with methanolic acetic acid (5 per cent). These eluates were then used for the determination of chemical and isotopic concentrations of the respective carbohydrates.

Details concerning the isolation procedure and chemical determination of the urinary carbohydrates will be published elsewhere. All determinations of radioactivity were carried out with a gas-flow counter using 'infinitely thin' layers of the compounds on polyethylene planchets, 2·5 cm. in diameter. The results are presented in Table 1.

Table 1. INCORPORATION OF CARBON-14 ACTIVITY IN VARIOUS COMPOUNDS RELATED TO THE RIBOSE POOL AFTER INJECTION OF CYTIDYLIC ACID-^{14}C (UNIFORMLY LABELLED)

Source	Compound isolated	Micromolar carbon-14 activity (c.p.m./μM)
Liver	Ribonucleic acid nucleotides	
	Cytidylic acid*	185
	Uridylic acid	120
	Adenylic acid	44
	Guanylic acid	40
	Acid-soluble nucleotides (free)	
	Adenylic acid	30
	Uridylic acid	300
	Glycogen (as glucose)	1
Urine	Imidazole acetic riboside	320
	Ribulose	305
	Xylulose	360
	Glucose	47

* The micromolar carbon-14 activity ratio of cytosine/ribosyl moiety was 0·31.

The following conclusions have been drawn from the results obtained: (1) The findings suggest the occurrence of transfer of ribosyl residues of cytidylic acid to imidazole acetic riboside as well as to free and ribonucleic acid-bound uridylic and adenylic acid in the liver. (2) The micromolar carbon-14 activity of the free urinary pentoses equals approximately that of the ribosyl moiety of imidazole acetic riboside, suggesting that incorporation of carbon-14 into the latter ribosyl moiety has occurred largely by way of phosphorolytic cleavage followed by pentose interconversions. (3) The results indicate that the contribution of cytidylic acid ^{14}C (uniformly labelled) to the labelling of purine nucleotides in the liver, either free or bound to ribonucleic acid, is of minor importance. (4) The low isotope concentration of urinary glucose suggests that the carbon atoms of the ribosyl

moiety are probably not in equilibrium with the carbon atoms of glucose.

We are indebted to Dr. H. Tabor for making available some unpublished information regarding imidazole acetic acid and imidazole acetic riboside.

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Selenium and Liver Necrosis in the Hyperthyroid Rat

It is well known that dietary deficiencies can be seriously aggravated by the induction of a hyperthyroid state. Recently it has been shown[1-3] that selenium significantly prolongs the survival-time of rats and prevents the onset of the liver necrosis which follows the ingestion of a diet containing yeast as the only source of protein. This protective effect of selenium resembles that shown by a number of apparently unrelated substances such as methionine, cystin, vitamin E, methylene blue and methylthiouracil, the mode of action of which is not understood. Unpublished observations, made in the course of a systematic investigation into the effects of various hormonal and nutritional stimuli on the course of liver necrosis, had suggested that it might be possible to distinguish between a true protective effect and a 'non-specific', indirect effect of the substances tested by the induction of a hyperthyroid state. Methylthiouracil, for example, which protects the euthyroid weanling rat against the onset of liver necrosis, was ineffective in litter-mates made hyperthyroid by the simultaneous addition of thyroid powder to the diet. A somewhat similar effect was seen if methylene blue was given, in contrast to the persistence of the protective effect obtained if vitamin E was used. In the light of these considerations it was thought of interest to see how the induction of a hyperthyroid state would affect the protective effect of selenium in dietary liver necrosis.

Male litter-mate rats of a strain bred in the Department of Anatomy, Birmingham, were weaned on the twenty-first day of life, the first day of the experiment, and were fed the 'necrogenic yeast diet' of Lindan and Himsworth[4] to which thyroid powder and sodium selenite had been added. The dose of selenium was kept constant at a level of 0·00002 per cent, but the level of thyroid powder was increased from 0·2 per cent (Exp. 1) to 0·3 per cent (Exp. 2) and 0·5 per cent (Exp. 3). All animals were kept in individual cages with raised screen floors, and were allowed to die spontaneously. The survival times and the incidence of liver necrosis are presented in Table 1. It can be seen that the induction of hyperthyroidism significantly accelerated the onset of liver necrosis, but that despite the presence of even a severe hyperthyroid state (Exp. 3), the small amount of selenium given prevented the development of dietary liver necrosis. Although the difference in the survival times of the rats fed the highest amount of thyroid powder with and without selenium was not significant, the absence of liver necrosis was striking. This protective action of selenium, in the presence of varying degrees of hyperthyroidism, is suggestive of a direct effect of selenium, and is best interpreted as the alleviation of a true deficiency. In view of the observations of Bunyan, Edwin and Green[2] on the protective effects of trace elements other than selenium, it would be of interest to see what effect the induction of a hyperthyroid state would have on the action of these trace elements.

Table 1. The Effect of Varying Levels of Thyroid Hormone with and without Selenium on the Survival Time (in days) of Litter-mate Rats fed the 'Necrogenic Yeast Diet'.
(Incidence of liver necrosis in parentheses)

Level of thyroid hormone	No. of animals	Necrogenic diet	Necrogenic diet plus thyroid hormone	Necrogenic diet plus thyroid hormone plus sodium selenite (0·00002 per cent)
Exp. 1: 0·2 per cent	7	40·4±5·42 (7/7)	25·0±1·02 (7/7)	59·4±9·48 (1/7)
Exp. 2: 0·3 per cent	7	29·3±1·25 (7/7)	19·6±0·68 (7/7)	33·9±3·54 (0/7)
Exp. 3: 0·5 per cent	8	23·3±2·33 (8/8)	16·7±0·50 (8/8)	20·5±2·19 (0/8)

Another point of interest is the effect of supplements of selenium on the course of the hyperthyroid state itself. Although the addition of thyroid powder to the diet significantly ($P < 0·001$) hastened the onset of liver necrosis in all the animals, increasing the dose of thyroid powder from 0·2 to 0·3 or 0·5 per cent had no significant effect on the survival times if each group was compared with the untreated litter-mate controls. (The spontaneous decrease in the survival times of the untreated controls of Exps. 1–3, seen in Table 1, is purely accidental.) This is in contrast to the obvious decrease in survival times found with increasing doses of thyroid hormone, if selenium is given in the diet as well. By comparison with the litter-mates given thyroid only, the regression was significant at the 5 per cent level using a 'two-sided' test. This observation again suggests that selenium acts by alleviating a dietary deficiency, and underlines the caution which is indicated if the effects of the pure, uncomplicated hyperthyroid state are to be clearly assessed.

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Utilization of the Carboxyl Group of Glycine for the Synthesis of the Amino-Acids of Silk by *Bombyx mori*

When fasting and ready to spin their cocoons, five silkworms were each injected with 112 μgm. (2·1 μc.) of glycine-1-^{14}C.

Fibroin was isolated from the cocoons by the method described by Dunn *et al.*[1]. The four amino-acids—tyrosine, glycine, alanine and serine—were then isolated from the hydrolysed fibroin, using a modification of Stein and Moore's procedure[2]: the hydrolysed fibroin was freed of excess hydrochloric acid by repeated evaporation and then by percolating through a bed of 'Amberlite' *IR* 120 (H+). The amino-acids adsorbed on the resin were eluted with 3 *N* ammonia, which was then evaporated *in vacuo*. At this stage, the tyrosine was removed by filtration and purified by crystallization and finally by chromatography on a starch column, with butanol/water as solvent[3]. Tyrosine was completely radio-inactive. Glycine was precipitated as glycine nitronaphthalene sulphonate, alanine as azobenzene-*p*-sulphonate and serine as *p*-hydroxyazobenzene-*p*-sulphonate. The amino-acids were obtained by passing the sulphonates through an 'Amberlite' *IR* 120 (H+) column and then eluting with 3 *N* ammonia. They were crystallized several times in water–ethanol–diethylether.

The specific activities of the sulphonates and of the derived amino-acids remained constant throughout the crystallizations. The chemical purity of each amino-acid was checked by Kjeldahl nitrogen analysis and by paper chromatography in butanol/hydrochloric acid and in phenol/water. They were then oxidized and converted to barium carbonate. The radioactivity measurements were performed with a thin mica-window Geiger counter on barium carbonate deposits. Each amino-acid was decarboxylated with ninhydrin[4]. The carbon dioxide evolved was trapped in sodium hydroxide solution and converted to barium carbonate. The radioactivities of the isolated amino-acids and of their carboxyl groups, corrected for background and self-absorption[5], are summarized in Table 1.

Table 1

	Specific activities		Total activity per cocoon (counts/min.)
	Amino-acid (counts/min./mmole)	Carboxyl group (counts/min./m.equiv.)	
Injected glycine	$2·7 \times 10^8$	$2·7 \times 10^8$	
Isolated glycine	196,000	196,000	81,500
Isolated serine	65,700	63,600	7,500
Isolated alanine	18,200	18,600	5,400
Isolated tyrosine	0	0	0
			94,400

Total activity injected per worm, 400,000 counts/min.

From these results, one can conclude that: (1) One quarter of the total activity injected appeared in silk fibroin. (2) The injected glycine was found diluted about one thousand-fold in the silk, which was most probably not uniformly labelled. (3) Direct conversion of glycine to serine keeping the label in the C-1 position occurs in the silkworm. It is probably the result of the addition of a one-carbon unit as shown in mammals, birds and micro-organisms. (4) There is also a conversion of glycine to alanine which might proceed through serine and pyruvic acid. Whatever the steps of this transformation are, the reactions involved must introduce the C-1 of glycine exclusively into the carboxyl group of alanine. (5) Tyrosine has not incorporated any radioactivity from glycine-^{14}C, whereas in a previous communication we have shown a direct conversion of phenylalanine to tyrosine[6]. This seems to indicate that the phenylalanine–tyrosine pair is essential to the silkworm.

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Utilization of Formate for the Biosynthesis of Glycine Carbon-1 and -2 in *Bombyx mori*

Just prior to spinning their cocoons, each of twenty silkworms was injected with 1·7 mgm. (25 μc.) of formate labelled with carbon-14. The fibroin, isolated by the method of Dunn *et* al.[1], was hydrolysed and the glycine isolated as nitronaphthalene sulphonate. This salt was recrystallized several times, then dissociated on a 'Dowex' 50 column; free glycine was eluted with 3 *N* ammonia and crystallized in water/ethanol/diethylether. Its chemical purity was checked by paper chromatography in two different solvents (phenol/*iso*propyl alcohol/water and butanol/acetic acid/water). The specific radioactivities of the nitronaphthalene sulphonate and of the free glycine remained constant throughout the recrystallizations.

The isolated glycine was decarboxylated[2]; C-1 was isolated as barium carbonate and C-2 as formaldimedone. The specific activities of the isolated glycine and of its two carbons are shown in Table 1; all determinations were performed with a thin mica-window Geiger counter on barium carbonate deposits (glycine and formaldimedone were oxidized and converted to barium carbonate before the assays) and the results corrected for background and self-absorption.

The degradation procedure was checked on synthetic glycine-1-^{14}C and glycine-2-^{14}C (Table 1).

It can be concluded that formate carbon is utilized for the synthesis of glycine C-1 and C-2 in *Bombyx mori*. 1·5 per cent of the injected radioactivity appeared in the fibroin glycine, while 2 per cent was found in fibroin serine which had a specific activity about six times greater than glycine.

Several biochemical pathways, known in other organisms, can be suggested to explain these results. Further work, namely the analysis of the distribution

Table 1. Specific Activities
(counts/min./mmole or m.equiv.)

	Isolated	1-^{14}C	2-^{14}C
Glycine	68,400	33,600	280,000
C-1	20,300	33,800	158
C-2	43,500	42	277,000

of carbon-14 in serine and alanine isolated from the silk fibroin, can help us to decide which of these routes is the most important in *Bombyx mori*. We already know that the administration of glycine-1-^{14}C is not followed by a redistribution of the labelled carbon between the two carbons (see preceding communication).

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Cellulolytic Activity of Phytopathogenic Bacteria

As the great majority of phytopathogenic bacteria are extracellular parasites occupying chiefly the vessels and the intercellular spaces, and causing vascular diseases, soft-rots, spot diseases, etc., the ability to decompose the surrounding walls composed of pectin and cellulose is supposed to be an important factor controlling the destruction and/or enlargement of the tissues attacked. Although Husain and Kelman[1] reported the presence of cellulase in diseased tomato tissues infected by *Pseudomonas solanacearum*, our knowledge of the cellulolytic enzymes is poor in comparison with that in the field of pectolytic enzyme studies of plant pathogens.

We have sought evidence *in vitro* as to whether cellulolytic enzymes are produced by other phytopathogenic bacteria. Bacterial species or isolates used were from our collections in Japan. For the recognition of cellulolytic enzymes carboxymethylcellulose gel medium was used as stab cultures and observed periodically for three weeks at an incubation temperature of 30° C. When the enzymes were produced, stratiform liquefaction of the gel followed the growth of bacterial species inoculated. The carboxylmethylcellulose gel medium was prepared as follows: 2 per cent of carboxymethylcellulose (Koso Chem. Co., Ltd., Tokyo) was dissolved in hot basal medium (70° C.) such as bouillon, potato decoction, synthetic solution *A* (ammonium dihydrogen phosphate, 1 gm.; potassium chloride, 0·2 gm.; magnesium sulphate, 0·2 gm.; distilled water, 1 l.); synthetic solution *B* (ammonium nitrate, 1 gm.; potassium hydrogen phosphate, 1 gm.; magnesium sulphate, 0·2 gm.; distilled water, 1 l.); or synthetic solution *C* (Uschinsky's solution without glycerol), then heated almost to boiling point and stirred sufficiently to form a homologous gel. The mixtures were placed in tubes and autoclaved at 15 lb./in.^{2} for 10 min. Tests were made with 13 species of *Pseudomonas*, 7 species of *Xanthomonas*, 2 species of *Erwinia*, 1 species of *Agrobacterium* and *Corynebacterium*, including various isolates of each species.

Prompt liquefaction of the gel was observed in bouillon and potato decoction cultures after 3–5 days, while in synthetic media the gel was liquefied very slowly and some isolates showed only partial liquefaction even after three weeks. The liquefying species or isolates grew well throughout the dissolved layers of gel. Growth of the non-liquefying ones was moderate on the gel surface in bouillon and potato decoction, but feeble or absent in synthetic media.

The results, obtained from potato-decoction gel cultures, showed that cellulolytic enzymes are produced from *Ps. panici* (syn. *Ps. setariae*), *Ps. solanacearum*, *Xanthomonas campestris*, *X. citri*, *X. nigromaculans*, *X. oryzae*, *X. pisi* (a new species, not reported), *X. pruni*, *X. vesicatoria*, *Erwinia carotovora* (including *E. aroideae* as a synonym), *E. milletiae*, *Corynebacterium sepedonicum*, but not from *Ps. aeruginosa*, *Ps. andropogoni*, *Ps. cichorii*, *Ps. eriobotryae*, *Ps. iridicola*, *Ps. maculicola*, *Ps. marginalis*, *Ps. marginata*, *Ps. phaseolicola*, *Ps. syringae*, *Ps. tabaci*, *Ps. theae* and *Agrobacterium tumefaciens*.

In the case of *X. oryzae*, *E. carotovora* and *Ps. solanacearum*, the rapidity of liquefaction varied with the kinds of isolates used.

The pathological significance and biochemical characteristics of the cellulolytic enzyme produced by these bacteria will be discussed elsewhere.

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The Kidney and Erythropoiesis

It has been pointed out[1,2] that, in the dog, bilateral nephrectomy abolishes erythropoiesis, and it was suggested that the kidney produces a factor stimulating red blood cell formation. The experimental result did not definitely exclude retention of some toxic substance that inhibits the erythropoiesis, since the nephrectomized animals were still uræmic (blood urea level at about 300 mgm. per cent) despite peritoneal dialysis.

In further experiments an attempt was made to dissociate a toxic effect from the lack of some erythropoietic factor of renal origin. Thus, erythropoiesis was studied in a group of eight dogs submitted to bilateral ureter ligation. This group was compared with one group of seven intact and one group of eight bilaterally nephrectomized animals.

Bone-marrow samples were examined every other day before and after surgery. 72 hr. after surgery, 5 μc. of iron-59, previously incubated in 20 ml. plasma, were given intravenously. The uptake of iron-59 into erythrocytes was measured in eight dogs during the three following days.

Five dogs lived long enough to allow studies of the maximal incorporation of iron-59. The dogs with ligated ureters as well as the nephrectomized ones refused food, and were given two or three daily peritoneal dialyses, thus reaching similar levels of toxic retention and malnutrition.

Despite these conditions, the following experiments show that erythropoiesis is almost normal in animals with ureteral ligation, showing that the absence of a kidney-factor is responsible for the impaired erythropoiesis in nephrectomized dogs.

The disappearance curves of iron-59 from the plasma are similar in normal dogs (39–153 min.) and in those with ligated ureters (64–171 min.). The average time at which half the radioactivity initially present has disappeared ($T/2$) is 299 min. in the nephrectomized, 89 in the normal animals and 96 in those with ligated ureters.

The rate of turnover of plasma iron is higher in animals with ligated ureters (0·25–0·85 mgm./kgm./day; mean, 0·48) than in nephrectomized ones

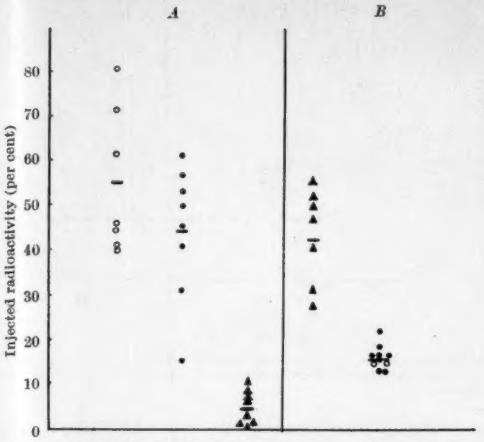

Fig. 1. (*A*) Uptake of iron-59 into erythrocytes. ○, Normal dogs 72 hr. after injection of iron-59; ●, dogs with ligated ureters 72 hr. after injection of iron-59; ▲, maximal uptake in nephrectomized dogs; —, mean. (*B*) Uptake of iron-59 into liver. ○, Normal dogs; ●, dogs with ligated ureters; ▲, nephrectomized dogs; —, mean

(0·09–0·49 mgm./kgm. day; mean, 0·24); the differences observed are statistically significant ($P < 0·01$). It is slightly lower than in normal animals (0·25–0·92 mgm./kgm./day; mean 0·64) but these differences are not significant ($0·1 < P < 0·2$).

The incorporation of iron-59 into red cells three days after injection of the isotope is almost the same in dogs with ligated ureters (15·6–60·9 per cent; mean, 44·1) as in normal animals (40–80·8 per cent; mean, 55·3), while it is less than 12 per cent in the nephrectomized dogs, 8 and even 10 days after the isotope administration. Maximal incorporation averages about 70 per cent in the normal and 61 per cent in the five dogs with ligated ureters (Figs. 1 and 2).

Our observations included an estimation of erythropoiesis by post-mortem measurements of radioactivity in the liver (Fig. 2). This radioactivity varies from 27 to 55 per cent (mean, 43·3 per cent) of the injected tracer dose in the group of seven bilaterally nephrectomized dogs and from 13 to 22 per cent (mean, 16·1 per cent) in the control group of dogs with ligated ureters and in two normal dogs. This suggests that in the controls iron-59 is chiefly deposited in erythropoietic organs. We also regard as noteworthy the persistence of erythroblasts in the bone-marrow of dogs with ligated ureters, since these elements disappear three days after bilateral nephrectomy.

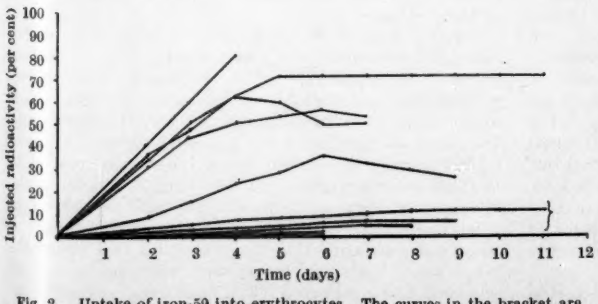

Fig. 2. Uptake of iron-59 into erythrocytes. The curves in the bracket are for nephrectomized dogs, the others for dogs with ligated ureters

These observations lead to the conclusion that the kidney produces an erythropoietic-stimulating factor, or transforms some precursor into an active agent. Besides this, it was shown that retention of toxic products does not impair erythropoiesis.

Our results agree with those of Jacobson[3] working on rats, but diverge from the observations of Mirand and Prentice, who noted an erythropoietic response in anoxic nephrectomized rats[4].

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Effect of Drugs on Conditioning and Habituation to Arousal Stimuli in Animals

Previous studies[1,2] using the feline *encéphale isolé* of Bremer have shown differential effects of certain drugs on the thresholds for electrocortical activation and behavioural arousal from sleep produced by auditory stimulation. In order to confirm and extend these results further experiments were carried out in conscious, chronic cat preparations carrying permanently implanted cortical recording electrodes[3]. For recording purposes these animals were placed in a constant-environment chamber fitted with a one-way glass window. Auditory stimuli were presented from a loudspeaker fitted in a side wall of the chamber, and the threshold for arousal was taken as the intensity of stimulation necessary to bring about abrupt desynchronization of the electrocorticogram and behavioural arousal.

It is clear that in any comparative study of the changes produced by drugs in the behavioural and electrocortical arousal reaction evoked by repeated sensory stimulation, we must take into consideration the normal processes which occur simultaneously. For example, in the present study the thresholds for arousal produced by a given auditory stimulus were not the same in every animal, and in any one animal they tended to fluctuate from day to day. In addition, the thresholds for a particular stimulus, although remaining constant when determined two or three times over a 4-hr. period, tended to increase when the stimulus was continually repeated over a similar period of time.

Habituation of the arousal reaction therefore developed very rapidly in these preparations where minimal intensities of auditory stimulation were employed, and it was found that the thresholds for auditory-induced arousal responses were only constant from approximately the first to the fifth presentation. This does not present a very stable base-line on which to test the effects of incremental doses of drugs. Sharpless and Jasper[4], however, have shown that habituation to a stimulus may be overcome by positive conditioning, and

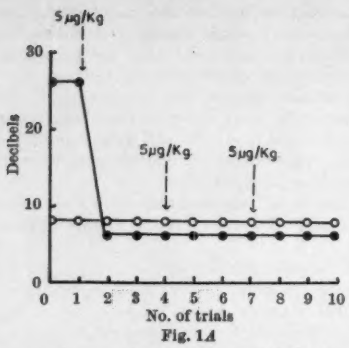

Fig. 1A

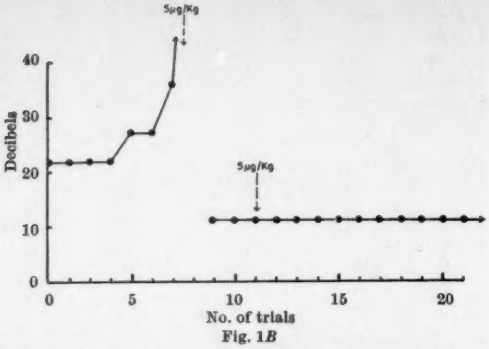

Fig. 1B

Fig. 1. *A*, The effect of lysergic acid diethylamide on conditioned and unconditioned auditory-induced arousal responses. *B*, The effect of lysergic acid diethylamide on habituation of the arousal reaction. ●, Threshold for unconditioned arousal; ○, threshold for conditioned arousal

therefore all preparations used in this study were conditioned to arouse upon the presentation of a specific tone. The conditioned response, consisting of both electrocortical desynchronization and behavioural arousal from sleep, was obtained by pairing an electric shock with the particular tone chosen. In doing this it was found that the arousal thresholds remained stable from day to day and the stimulus could be repeatedly presented at short intervals for something like 30–40 trials before extinction took place. It is interesting to note that during the conditioning trials the thresholds for electroencephalographic and behavioural arousal produced by the conditioned stimulus progressively decreased in every animal to a level approaching the threshold of hearing.

In all the experiments carried out with chronic unrestrained preparations the drugs were injected by the intraperitoneal route. Chlorpromazine in doses of 5–10 mgm./kgm. produced a rise in the thresholds for conditioned and unconditioned auditory-induced arousal responses. Following a total dose of 15–20 mgm./kgm., the conditioned as well as the unconditioned arousal response was blocked completely even when the intensity of the stimulus was considerably increased above control levels. At this point visual and tactile stimuli which normally evoked arousal responses failed to do so.

Reserpine also produced an increase in the arousal thresholds. Since this drug appears to have a delayed action incremental doses were not given. Instead, a single dose of 200 or 250 μgm./kgm. was injected and the thresholds then checked every half-hour over a 5-hr. period. The effects of reserpine were very slow to appear, and no significant effect was observed until 1–1½ hr. after the injection, when the thresholds for conditioned and unconditioned auditory-induced arousal showed a slight rise. After 2–3 hr., however, a dissociation of the threshold/time response curves became apparent. The thresholds for the unconditioned response rose progressively until 3½ hr. after the injection arousal produced by the neutral stimulus was blocked completely. On the other hand, the threshold for the conditioned response remained constant or rose a further step but in no case was the conditioned response blocked by reserpine. Moreover, the animal still responded to novel stimuli, which suggests that the blocking of the unconditioned response might be due to habituation.

The effect of lysergic acid diethylamide was tested on conditioned and unconditioned arousal responses. In addition, the animal was also habituated to an auditory stimulus by continued presentation over a short period of time. After an initial dose of 5 μgm./kgm. of lysergic acid diethylamide conditioned arousal responses remained unaffected but the threshold for the unconditioned response fell sharply (Fig. 1*A*). Similarly, the stimulus to which the animal had become habituated now evoked a marked response. The intensity of the stimulus needed to produce this effect was also much lower than the original level (Fig. 1*B*). Following a total dose of 10–15 μgm./kgm. of lysergic acid diethylamide the animal became more responsive to sensory stimulation and remained alert for long periods. The thresholds for arousal, however, did not show any further change.

The arousal value of a sensory stimulus depends upon the significance which is attached to it by the animal. Positive conditioning increases the significance, whereas during habituation there is a loss of significance. In these experiments chlorpromazine appeared to simulate the effects of habituation for a wide range of sensory stimuli, the animal becoming indifferent to stimuli which previously had evoked electrocortical activation and behavioural arousal. In contrast, lysergic acid diethylamide appeared to increase the significance of most sensory stimuli to a level similar to that achieved by positive conditioning for any given stimulus. The fact that both lysergic acid diethylamide and chlorpromazine produced no marked effect on the thresholds for arousal evoked by direct stimulation of the brain stem reticular formation[2], and yet have an effect on auditory-induced arousal responses, emphasizes the importance of the neural mechanisms regulating the inflow of sensory information in relation to the action of these drugs.

The blocking of the unconditioned arousal responses following reserpine can, as already stated, be explained on the basis of habituation, since novel stimuli were still capable of producing arousal. Thus in contrast to chlorpromazine, it would appear that the sedation produced by reserpine does not seem to be entirely dependent upon the action related to the inflow of impulses into the brain stem from the classical sensory pathways. The site of action of reserpine cannot be defined at this stage, but it is interesting to note that reserpine did not block the conditioned arousal responses, whereas numerous workers have reported that this drug severely depresses conditioned avoidance behaviour[3]. The use of

conditioned arousal responses eliminates a task involving muscular co-ordination, and it may well be that responses of this sort may help to distinguish more clearly the selective effects of some drugs from a more diffuse and non-specific action of others.

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Lenticular Effect in Mice of Some Morphine-like Drugs

DRUG-INDUCED opacities of the lens of the eye have been recorded by Busche[1] using nitrophenol compounds in chicken. He was unable to produce this in any other small animals except in one particular strain of mice. While investigating the acute toxic effects of a series of reversed esters of pethidine, we observed that a number of these also produced an opacity. This was completely reversible and has been obtained by using other analgesic drugs in several strains of mice.

Fig. 1 shows the typical reaction seen in the eyes of mice after subcutaneous injection of 2 mgm. of (DL)-methadone hydrochloride. All doses mentioned are expressed as mgm./100 gm. of body-weight, and the mice used (both sexes) weighed 18–22 gm. The cloudiness begins to appear at 15 min., reaching a maximum in 50 min., when it slowly disappears. 3 hr. later, the eye is clear again. Smaller doses produce less effect. The opacity develops more slowly with morphine, reaching a maximum in 75–90 min. The effect can be produced in rats but less readily. This species is more sensitive to other toxic actions of these drugs so that the blood concentration to produce an opacity would usually be lethal.

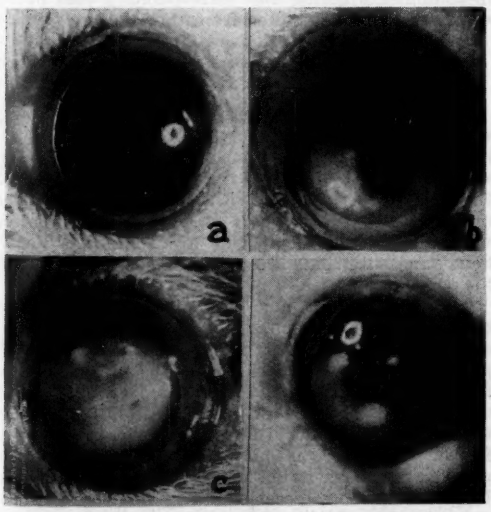

Fig. 1. Various degrees of eye opacity developing in the lens after subcutaneous injection (2 mgm./100 gm.) of (DL)-methadone hydrochloride: (*a*) normal eye; (*b*) 30 min.; (*c*) 50 min.; (*d*) 75 min.

The cloudiness developed in the lens while the cornea remained clear when the eye was viewed through a slit-lamp microscope. Removal of the lens confirmed the site of the opacity. Further investigation has shown that in the intact animal clouding takes place on the anterior surface of the capsule while the lens itself remains transparent. In isolated normal lenses exposed to the same drugs, similar changes occur, but the whole capsule is involved.

A range of drugs has been tested to determine whether the production of this opacity is confined to a certain class of compound. This was found to be the case with narcotic drugs, and particularly with the potent analgesic members of this group. The exceptions were cocaine and papaverine, which had only one-tenth to one-twentieth of the activity of methadone. This effect was produced in at least 20 per cent of the mice by subcutaneous injection, in doses less than 5 mgm., of pethidine hydrochloride and three of its reversed esters (to be published in detail elsewhere); of morphine sulphate and some of its structural analogues, and of (DL)-methadone hydrochloride. Of those tested, the more active the drug was as an analgesic the more readily it produced an opacity.

No effect could be obtained by sublethal doses of the following drugs:

Codeine phosphate	Pentobarbitone sodium
Apomorphine hydrochloride	Cyclobarbitone sodium
Mepyramine maleate	Phenobarbitone sodium
Diphenhydramine hydrochloride	Acetyl-salicylic acid
Histamine acid phosphate	N-acetyl-*para*-amino phenol
Atropine sulphate	Phenacetin
Physostigmine salicylate	Lignocaine hydrochloride
Quinidine sulphate	Amethocaine hydrochloride
Amiphenazole hydrochloride	Procaine hydrochloride

This additional activity of these analgesic drugs has been studied in more detail. In Table 1 a comparison is made of the dose which will produce analgesia in 50 per cent of the mice (*ED*50) as determined by the 'tail clip' method[5], the dose which will kill 50 per cent of the mice (*LD*50) and the dose which will cause cloudiness in 20 per cent of the mice (minimum opacity dose). In each case the dose required to produce the opacity is greater than the corresponding *ED*50, but less than the *LD*50. By changing from the subcutaneous to the intravenous route, clouding of the lens, analgesia and toxicity are increased by all three drugs. When any of these are given intraperitoneally they become less active both as analgesics and in their effect on the eye, yet they are more toxic. Thus it appears that the production of opacity follows the degree of analgesia more closely than the lethal action of these drugs.

The lenticular opacity produced by analgesic drugs can be prevented by the simultaneous injection of

Table 1. MINIMUM DOSES TO PRODUCE OPACITY AND ANALGESIA COMPARED WITH THOSE FOR LETHAL EFFECTS BY DIFFERENT ROUTES

Analgesic drugs	Route	*ED*50 (mgm./100 gm.)	Minimum opacity dose (mgm./100 gm.)	*LD*50 (mgm./100 gm.)
Morphine	s.c.	0·5	4·0	50
	i.p.	0·8	6·0	31
	i.v.	0·4	2·5	15
Pethidine	s.c.	1·4	5·0	17
	i.p.	3·1	7·5	12
	i.v.	1·2	2·0	4
Methadone	s.c.	0·3	1·0	4·0
	i.p.	0·4	1·5	2·8
	i.v.	0·3	0·75	1·5

small doses of nalorphine. Furthermore, if the effect has already developed, this antagonist will cause it to disappear in less than one-fifth of the normal time. Nalorphine itself can produce this opacity also but only with doses greater than 50 mgm. As expected, the cloudiness produced by cocaine could not be antagonized in this way.

The modification of this effect by other agents is being investigated. An examination of the actions of these drugs on enucleated lenses is also being carried out because in contrast to the *in vivo* experiments such opacities can be produced by compounds differing widely in pharmacological properties. A detailed report of this work will be published elsewhere.

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Dependence on Age of the Diameter of the Pupil in the Dark

The dependence of the diameter of the pupil of the human eye in the dark on the age of the subject, derived from a large amount of statistical material, is important not only for ophthalmology and neurology but also for physiological and practical optics.

Very little work has been done on this subject, however, and in ophthalmological and optical literature therefore only the values of old measurements after Trendelenburg[1-5] are given (Fig. 1).

In 1950, Birren *et al.*[6] published values for the vertical diameters of the left eyes of 216 subjects in the dark after 90 sec. adaptation, obtained by

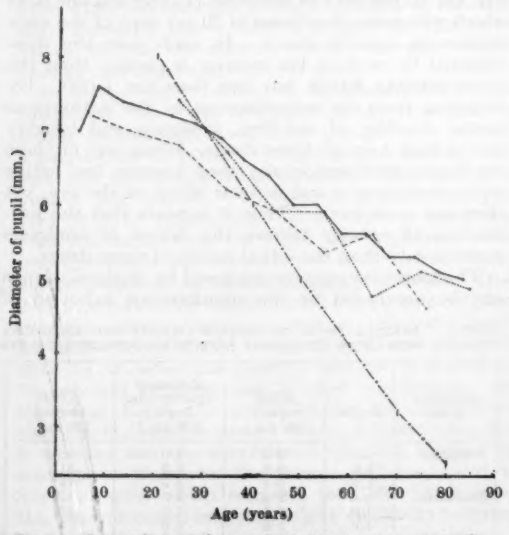

Fig. 1. Mean values of the apparent diameter of pupil in the dark as a function of age according to: Trendelenburg, —•—•—; Birren, ...; Seitz, — — —; Kadlecová, Peleška and Vaško, ————

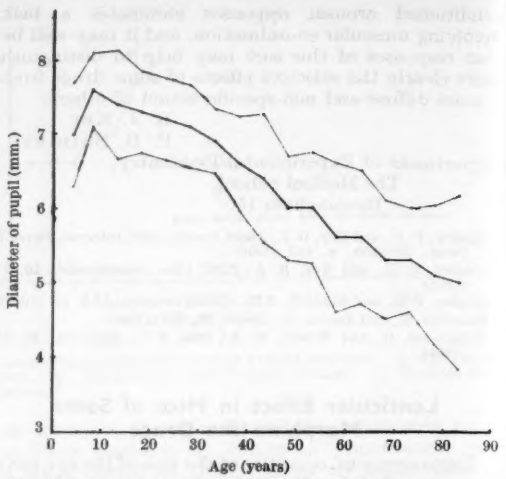

Fig. 2. Mean values of diameter of pupil in the dark with corresponding root-mean-square errors of one measurement as a function of age according to Kadlecová, Peleška and Vaško

flash photography with visible light. These differed substantially from Trendelenburg's values (Fig. 1). Since 1946 we have been measuring the diameter of the pupil in the dark by infra-red radiation—thus eliminating all effects of visible light—with an image converter[7]. The mean values obtained by us for 906 horizontal diameters of both pupils of 453 normal subjects in the dark after 15 min. adaptation are also plotted in Fig. 1. Each subject was clinically examined and cases with diseased iris and nervous system were eliminated.

Later, Seitz published[8] measurements on 208 subjects, made by flash photography in visible light after adaptation for 1 hr. in the dark. These have also been included in Fig. 1, after correcting the mean value of the diameter of the pupil for the age group 40–49 years from 5·1 mm. to 5·9 mm.

In Fig. 2 are plotted the mean values of our measurements giving the corresponding root-mean-square errors δ, calculated from the relation:

$$\delta = \pm \sqrt{\frac{\Sigma \Delta^2}{n - 1}}$$

A comparison of these results shows that for young subjects up to about thirty years of age our measurements give lower values than those of Trendelenburg, while from thirty upwards the values are higher and the differences increase with increasing age. The measurements of Birren *et al.* agree approximately with our measurements but are somewhat lower. Seitz's measurements are mostly lower than ours but his curve is practically parallel to our curve.

The accuracy of our method permitting visual observation of the infra-red image of the eye is certainly much greater than methods using flash photography in the dark, since the uncertainty in focusing the image of the pupil after a longer period of adaptation in the dark is removed. Other authors themselves point out the difficulty in maintaining focus[8]. Moreover, as our observations showed, the pupil in the dark is not absolutely at rest and can be seen to perform occasional very fine contractions. Our visual method enables such contractions to be eliminated and the real maximum diameter of the pupil to be measured. Our measurements showed

that the diameter does not depend on sex or on the colour of the iris. The diameters of the pupils of both eyes were found to be the same. We found, however (Fig. 2), a visible increase in the mean error (dispersion of values) with age.

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Influence of Hydrocortisone on the Action of Sodium on Isolated Rabbit Auricles

SZENT-GYÖRGYI[1] has demonstrated the importance of the 'intracellular ionic atmosphere' on the contraction of the cardiac muscle, and has suggested that adreno-cortical steroids may influence cellular activity by alterations in membrane permeability. It has also been shown by Selye and Renaud[2] that the action of electrolytes on the heart is influenced by what is termed the 'conditioning' effect of hormones. Further, Holland[3] has presented evidence to show that antiarrhythmic drugs act on the atria by depressing the transmembrane flux of sodium and potassium ions. In this connexion, it would be of interest to examine the effect of the steroid hormones on the action of the ions on the heart. It is well known that when the heart is kept in a medium containing sodium as the only ion it stops beating after some time. Later, when the medium is changed to Ringer solution, the beat recommences, presumably due to sodium extrusion. If a steroid hormone altered the permeability of the cell membrane, it would modify the action of sodium by interfering with sodium traffic across the membrane.

In order to examine this possibility, isolated rabbit atria were kept in oxygenated Ringer solution in a thermostatic organ bath at 37° C. and the contractions recorded on a kymograph. After obtaining normal contractions, the Ringer solution was replaced by physiological saline. There was inhibition of the atrial contraction within a short time. On replacing Ringer solution in the bath the contractions recommenced. Addition of hydrocortisone (kindly made available by Mr. A. V. Mody, Unichem Laboratories, Bombay) to the bath in quantities sufficient to give a final concentration of 25 μgm./ml. resulted in inhibition of the atria. The beats, however, recommenced on changing to fresh Ringer solution, but now replacement of the medium by sodium chloride solution did not result in an early inhibition of the contractions. The inhibitory effect of sodium was significantly postponed by an extremely short pretreatment with the steroid hormone. In fact, in some instances

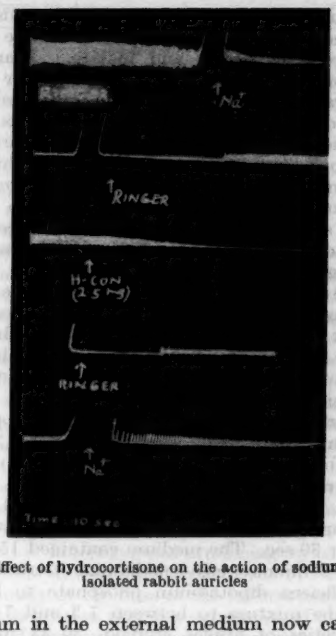

Fig. 1. Effect of hydrocortisone on the action of sodium ions on isolated rabbit auricles

the sodium in the external medium now caused an initial increase in the amplitude of the contraction of the atria. The results are shown in Fig. 1. It is suggested that such an action of the hormone could be due to altered myocardial excitability because of imprisonment of intracellular ions caused by a change in the cell membrane permeability by the steroid.

My thanks are due to Mr. N. M. Chavan for all the technical assistance rendered.

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Isolation of Active Mitochondria from Apples

IN recent studies on the physiology of ripening in fruits, attention has been focused on the possible relationship between phosphorylative processes and the climacteric rise in respiration[1–3]. Since many respiratory enzymes are located in the mitochondria, the isolation of these subcellular units in an active state is of great importance in such investigations. Although the apple is the classic object for studies in fruit physiology, attempts to prepare particulate fractions with mitochondrial activity from apples have not been successful. Lieberman[4] isolated particles with cytochrome oxidase activity by grinding apples in a medium containing *tris*-hydroxymethyl aminomethane at *p*H 9·2. By using a homogenizing medium buffered at *p*H 7 with 0·5 *M* phosphate, Neal and Hulme[5] obtained apple particles which oxidized succinate and malate to a slight extent, but only in the presence of the phenolic compound protocatechuic acid. Pearson and Robertson[2] isolated

apple particles that had a high endogenous oxygen uptake and that showed some oxidative activity with succinate, citrate and malate. Pearson and Robertson's[2] particles were obtained after a single centrifugation of the homogenate and possibly contained contaminating phenolic compounds. These compounds may have contributed in part to the endogenous oxygen uptake and, in the light of Neal and Hulme's[5] results, may also have been responsible for the oxidation of the added acids. In all these studies, stress has been laid on the necessity for counteracting the high acidity of the tissue when preparing mitochondria from apples.

I have overcome a similar difficulty in the banana[6], and prepared active mitochondria by incorporating sufficient dipotassium phosphate into the homogenizing medium to bring the *p*H of the homogenate to 7. When this method was applied to apples, active mitochondria were also obtained.

The procedure was as follows. Ripe apples were placed in a room maintained at about 1° C. at least 2 hr. before being used, and all subsequent manipulations were carried out at this temperature. 200 gm. of diced pulp were extracted with 300 ml. medium in a Waring blendor connected to a rheostat set at 40 V. for 30 sec. The medium contained 150 mmoles sucrose, 3 mmoles ethylenediamine tetraacetic acid and sufficient dipotassium phosphate to bring the *p*H of the mixture to between 7·3 and 7·4. With the varieties of apples studied, 30–33 mmoles dipotassium phosphate were needed for 200 gm. pulp. The mixture was pressed through a layer of muslin and centrifuged at 1,000*g* for 6 min. The supernatant was centrifuged at 20,000*g* for 15 min. The precipitate was suspended in 40 ml. of 0·5 *M* sucrose – 0·01 *M* phosphate, *p*H 7·4, with the aid of a Potter–Elvehjem homogenizer and recentrifuged at 20,000*g* for 15 min. The precipitate was finally suspended in 0·5 *M* sucrose – 0·01 *M* phosphate, *p*H 7·4, and made up to 4–8 ml. with the same solution. The resultant suspension, which was light yellow, dark yellow or yellowish green, depending on the variety of apple used, was tested for mitochondrial activity in a Warburg respirometer at 30° C.

Each Warburg vessel contained: 40 μmoles phosphate at *p*H 7·4; 15 μmoles magnesium sulphate; 6×10^{-5} μmoles cytochrome *c*; 4×10^{-4} μmoles cocarboxylase; 3 mgm. liver coenzyme concentrate; 2×10^{-3} μmoles adenosine triphosphate; 3 mgm. bovine plasma albumen; 40 μmoles glucose; 650 μmoles sucrose; 40 μmoles substrate and 0·5 ml. of the particulate suspension in a final volume of 2 ml. The sources of the biochemicals and the analytical procedures used are described elsewhere[6].

In the absence of added substrate, the apple particles had an oxygen uptake of 0–1 μl. per vessel. The oxidative activity of the particles towards various substrates is shown in Table 1. The succinoxidase activity of the particles isolated from each variety was high. Malate and α-oxoglutarate were oxidized by the particles at a much lower rate than succinate. The ability of the particles from Ohenimuri and York Imperial apples to oxidize citrate is doubtful; the particles from the other varieties oxidized citrate at a rate comparable to that with α-oxoglutarate or malate as substrate. No browning of the reaction mixture was ever observed, an indication that the oxidation of phenolic compounds was not taking place.

Table 1. Oxidative Activity of Mitochondria isolated from Various Apple Varieties. Conditions indicated in Text

Variety	Mitochondrial nitrogen per vessel (mgm.)	QO_2(N) with			
		Citrate	α-Oxoglutarate	Succinate	Malate
Golden Delicious	0·51	53	59	106	43
Granny Smith	0·62	44	66	139	62
Ohenimuri	0·20	10	60	220	60
Starking	0·21	86	76	276	133
White Winter Pearmain	0·38	39	63	158	39
York Imperial	0·23	13	39	169	56

The oxidation of pyruvate by these particles could not be demonstrated unequivocally; the oxygen uptake in the presence of pyruvate and catalytic amounts of succinate was only slightly higher than the oxygen uptake with succinate alone.

These apple particles differ from the preparations described in the literature[2,4,5] in having virtually no endogenous oxygen uptake, in their ability to oxidize four members of the tricarboxylic acid cycle, and in the independence of this oxidative activity from polyphenolase activity. It is hoped that further refinement of the procedures described above will lead to the isolation of apple cytoplasmic particles with a full spectrum of mitochondrial activity, as evidenced by their ability to oxidize pyruvate via the tricarboxylic acid cycle and to carry out the concomitant phosphorylations.

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Artificial Light and Sexual Maturity in the Fowl

In a recent communication[1] we outlined a general hypothesis to account for the relationship between day-length and sexual maturity in the fowl, *Gallus domesticus*. We have since conducted an experiment which offers striking evidence in support of the hypothesis that sexual maturity is affected by changes in day-length and not by the absolute day-length.

Four groups, each of 150 Rhode Island Red × Light Sussex pullets hatched on December 4, 1957, were reared under identical conditions except for light treatments as follows. Two groups served as controls and received natural daylight only (latitude, 51° 27′ N.): the other two groups were given supplementary lighting to provide continuous illumination during the first week of life and thereafter day-length was reduced by 35 min. each week to reach a level of 14 hr. 5 min. at 17 weeks of age. On April 3 (17 weeks) all four groups were transferred to laying cages where they have been treated uniformly in every respect. Artificial light was not used in the laying house until after the summer solstice, by which time all the birds were in lay.

Table 1. AVERAGE RESULTS TO 37 WEEKS OF AGE

	No. of pullets housed	Age at first egg (days)	Body-weight at: 20 wk. (gm.)	Body-weight at: 30 wk. (gm.)	Eggs per pullet housed: By grades (oz.) $< 1\frac{7}{8}$	$1\frac{7}{8}$–$2\frac{3}{16}$	$>2\frac{3}{16}$	Total
Controls	285	145·6	2,371	2,772	35·5	24·8	4·3	64·6
Lighted	291	169·7	2,222	2,867	18·3	37·4	7·9	64·1
Difference		24·1*	149†	95†	16·7†	12·6†	3·6†	0·5

* Significant, $P < 0{\cdot}01$. † Significant, $P < 0{\cdot}05$.

Average age at first egg is given in Table 1. It is clear that the artificial pattern of decreasing day-length delayed sexual maturity even though it involved the provision of more light than was available to the naturally lit controls. The possibility that long day-lengths, *per se*, inhibit sexual maturity has been eliminated by the work of Hutchinson[2] and others.

In this experiment the net increase in day-length experienced by the controls between hatching and sexual maturity was 6·67 hr. and the net increase experienced by the lighted groups was 8·02 hr. The expected difference in sexual maturity between them, on the basis of the regression coefficient calculated from previous results[1], would therefore be $1{\cdot}64 \times (6{\cdot}67 + 8{\cdot}02) = 24{\cdot}1$ days. That this agrees so exactly with the observed difference may be coincidental. However, the results of this experiment do agree quantitatively as well as qualitatively with the hypothesis already published. It remains to be seen whether our regression coefficient can be treated as a constant for all stocks.

To measure the benefits which accrue from using lights to delay maturity in pullets hatched in December, records of egg-production, egg-weight, body-weight and mortality will be kept to 450 days of age. Table 1 gives the results up to 37 weeks, and it is apparent that the light treatment has produced an improvement in rate of lay sufficient to offset the 3 weeks delay in maturity. Early egg-size has also been substantially increased, presumably because of the greater body-size eventually attained by the lighted groups.

Full details of this experiment, which is being conducted with the aid of funds provided by the Agricultural Research Council, will be reported elsewhere in due course.

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Male Sterility in *Brassica*

MALE sterility has been reported in thirty-one genera[1], but not previously in the genus *Brassica*. In the course of breeding work at this Station male sterile plants have been found in inbred material of three varieties of brussels sprout[2–4]. In one of these varieties one male sterile plant was also found in 5,000 non-inbred plants inspected[4].

Meiotic division in the male sterile plants proceeded normally, but in the majority of anthers pollen development ceased at the tetrad stage, after which the young pollen grains degenerated. At flowering time the anthers were shrivelled (2–4 mm. long). In about 1 per cent of anthers occurring at random on male sterile plants, about 10 per cent of the pollen tetrads continued development to produce apparently normal pollen grains. Such anthers developed to their normal length (10–15 mm. including filament) although they were emaciated and indehiscent. After teasing out such anthers and applying the contents to normal styles, no seed was obtained. The flowers of male sterile plants were usually, though not invariably, smaller and paler in colour than those of normal plants.

This male sterility was found to be inherited as a simple recessive at a single locus. The expression of dominance of male fertility was imperfect, about 25 per cent of heterozygotes producing up to six male sterile flowers (about 1 per cent of the flowers on the plant), usually at the base of the inflorescence. There was some indication that the expression of dominance was affected by temperature, since heterozygotes kept at 70° F. produced more male sterile flowers than others kept at about 55° F.

Male sterility is expected to be of use for the production of hybrid seed in the inbreeding and hybridization programme with brussels sprouts at present in progress at this Station.

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Nitrogen Fixation by Non-nodulated Plants, and by Nodulated *Coriaria arborea*

IN a recent communication, Bond[1] discusses the probability that nodulated plants of *Coriaria* fix atmospheric nitrogen in the same way as other non-leguminous nodulated plants with which he has worked. This supposition is confirmed by the results of a trial which was made during the course of other work using nitrogen-15. Wild seedlings of *C. arborea* about 6 in. high, each with a cluster of pink nodules 1–2 mm. long near the crown, were collected from a rocky roadside cutting near Nelson, and grown in quartz sand watered with a minus-nitrogen culture solution. Results from exposing these plants to an isotopically enriched atmosphere are given in Table 1. There was considerable fixation of nitrogen, which may have occurred in the leafy shoots as well as in the roots.

During the past four years I have been investigating the possibility of nitrogen fixation by non-nodulated plants which make vigorous growth in poor soils. Evidence, which is more fully presented and discussed

Table 1

Duration of exp. (days)	Atom per cent excess nitrogen-15 in atmosphere	Plant		Atom per cent excess nitrogen-15 plant material
12	15	*Coprosma robusta*	tops	0·19
			roots	0·012
7	31	*C. robusta*, shoots only		0·024
		C. robusta, shoots only		0·047
		Prunus armeniaca, shoots only		0·058
14	7	*Pinus radiata*	tops	0·056
			roots	0·029
9	About 15	*P. radiata*, root exposed only	tops	0·004
			roots	0·042
14	5	*Dactylis glomerata*	tops	0·05
			roots	0·52
18	16	*D. glomerata*	tops	0·016
			roots	0·225
10	About 10	*D. glomerata*, roots exposed only	tops	0·003
			roots	0·014
14	25	*Epilobium erectum*	tops	0·51
			roots	0·014
28	6	*E. erectum*	tops	0·07
			roots	0·07
18	6	*E. erectum*	tops	0·020
			roots	0·095
28	About 3	*Coriaria arborea*	tops	1·177
			roots	0·695

in another publication, has been gathered from three lines of inquiry :

(1) Records of field-experiments published by a number of different workers for the yield of various crops, in relation to fertilizer used and soil nitrogen, over periods of many years, have shown substantial gains of the order of 30–50 lb. nitrogen/acre/year in the absence of legumes or other nodulated plants. Records of native vegetation give similar figures for large, unexplained gains in soil nitrogen. For *Pinus radiata* plantations growing on sand dunes or depleted soils in New Zealand, I made measurements and analyses which showed a gain over twenty-five years of 38 lb. nitrogen/acre/year.

(2) Pot experiments with a number of non-nodulated plants grown in a strictly no-nitrogen medium, in the absence of non-symbiotic nitrogen-fixing micro-organisms, have shown substantial gains in nitrogen over periods of 6 months to 3 years.

(3) Experiments have been carried out with nitrogen-15 in which either whole plants grown in a minus-nitrogen culture in enclosed glass pots, or shoots and roots separately, were exposed to an atmosphere enriched in the heavy isotope. Significant gains in nitrogen-15 have been made by the growing plants, and some typical results are given in Table 1. Leafy shoots (tops) and roots were assayed separately ; figures for control material were 0·003–0·005 atomic per cent excess nitrogen-15 (all figures with respect to cylinder nitrogen).

The evidence from these three lines of investigation leads to the conclusion that a number of non-nodulated plants are able to utilize atmospheric nitrogen. In the case of *P. radiata* and cocksfoot grass, it appears likely that fixation is a function of the mycorrhizas, though it still has to be proved that bacteria in or on these fungal roots are not also implicated. In the case of fixation in the leafy shoots it is possible that bacterial glands are responsible for the effect, but it is also possible that some leaves may yet be found to have a capacity for using nitrogen gas in the absence of micro-organisms.

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Effects of Water-Strain on the Minimum Intercellular Space Carbon Dioxide Concentration Γ in Wheat Leaves

In a recent communication, Rees[1] reported that midday closure in the oil palm was associated with water-strain and correlated in extent with total evaporation. There was also a relation with air temperature showing striking stomatal closure between 30° and 35° C., strongly reminiscent of the results of Heath and Orchard[2] for the log Γ/leaf temperature relation in onion and coffee leaves and of those of Heath and Meidner[3] for the stomatal aperture/leaf temperature relation in onion leaves closed at the tip. Rees concludes : "Although increasing leaf temperature may cause stomatal closure, it is clear that midday closure of stomata may also be influenced by water-strain . . .". In work carried out with wheat leaves we found a relation between degree of water-strain and Γ (the minimum intercellular space carbon dioxide content[2]) which is very relevant to this conclusion.

It was found that when detached wheat leaves were subjected to different degrees of water-strain by placing their sheaths in mannitol solutions of different concentrations, Γ values changed very significantly even with leaf temperature and light intensity maintained constant (Table 1).

Table 1. Mean Γ Values (maintained for 20 min.), in Parts per Million of Carbon Dioxide, From Eight Wheat Leaves (Leaf temperature, 25° C. ; light intensity, 900 foot-candles ; relative humidity, 50 per cent)

Successive treatments	0·2 *M* mannitol	0·4 *M* mannitol
Water	78	77
Mannitol	94	116
Water	83	82

Significant difference for P 0·05 = 5·9 ; significant difference for P 0·001 = 10·6

Similar increases in Γ were obtained by withdrawing the water supply to produce water-strain, instead of using mannitol, and on restoring the water supply Γ gradually returned to its original level ; the increases recorded in Table 1 are not therefore simply attributable to the mannitol being metabolized by the leaf.

Porometer measurements showed that stomatal closing movements accompanied the increased Γ values produced by water-strain, and some re-opening occurred when Γ fell once more.

These results suggest the existence in the wheat leaf of a carbon dioxide-operated stomatal closing response to water-strain, similar to the carbon dioxide-operated response to high temperature in onion, and probably in coffee leaves, previously discussed[2,3]. In different species midday closure may be mediated by one or the other or both of these mechanisms. Wheat stomata have not in fact been recorded as showing midday closure, and information is not yet to hand as to whether wheat leaves show the sudden increase in Γ with temperature rise above 30° C. found with

onion and coffee; stomatal closure does, however, occur in response to dry air[4].

Special significance may be attached to a regularly observed initial decrease in Γ (of about 10 per cent) on placing the leaf sheaths in mannitol solution, which preceded the increase. This decrease was accompanied by the frequently recorded 'passive' initial stomatal opening on wilting. It is possible that epidermal shrinkage, perhaps due to the large 'motor cells', altered the amount of light reaching the chlorenchyma, for it was observed that in this condition the leaves appeared darker suggesting that more light was absorbed. Whatever the mechanism, however, such a temporary decrease in Γ would tend to accentuate stomatal opening—thus the temporary opening on wilting may, in wheat, be in part an effect due to carbon dioxide.

This work was carried out in the Research Institute of Plant Physiology of the Imperial College of Science and Technology, London, with the support of a grant from the Nuffield Foundation. Full experimental details will be published elsewhere in due course, and this line of investigation is being pursued further.

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Mode of Intercellular Transfer of Herpes Virus

In previous studies[1] on the growth of the *HFEM* strain of herpes virus in HeLa cells, attempts were made to estimate the proportion of infected cells by inoculating the intact cells on to the chorioallantois of fertile hens' eggs and determining the number which formed pocks. It is known that the chorioallantois is at least ten times more sensitive than HeLa cells to this strain of virus released from HeLa cells. Nevertheless, the proportion of infected (pock-forming) cells was much lower than would be expected from the deduced input of HeLa infective virus, and it was concluded that the cells might not survive long enough to make virus in this environment.

Later, Wildy *et al.*[2] cultured single cells in microdrops of medium and determined the number which released pock-forming virus; the proportion was higher but still less than would be expected, and not related to input of virus per cell over the range tested.

The development by Farnham[3] of a plaque technique in monolayers of HeLa cells under fluid medium has since allowed more accurate determination of the numbers of infecting particles in relation to number of cells. It has also permitted the direct estimation of the number of infected cells by their ability to form plaques (that is, infective centres).

The media and other solutions used and the techniques for preparing cells and virus were as described elsewhere[1,3]. In several experiments monolayers of $3–5 \times 10^5$ HeLa cells were exposed to 5×10^5 HeLa plaque-forming units of virus for 2 hr. The residual virus was removed by treating the cells with antiserum, which was itself removed by washing. This resulted in an input of $2{\cdot}2 \times 10^3$ plaque-forming units per monolayer or 0·44–0·78 per cell. The cells, containing virus in the lag phase of growth, were then suspended in sodium ethylenediamine tetraacetate, counted, diluted in maintenance medium, and lots of 50 cells were inoculated on to uninfected monolayers of HeLa cells. Plaques were counted microscopically after 3 days.

In the pooled results of five similar experiments with 27 readings the mean number of plaque-forming cells was 21·8 (standard error ± 1·85) or 43·6 per cent. Variation in the number of cells inoculated gave proportional variation in the number of plaques. When the cells were disrupted by freezing before plating less than 2 per cent formed plaques. The mean input for the five experiments was 0·59 plaque-forming units per cell which, according to Poisson distribution, should result in infection of 45 per cent of cells, so that the method apparently detected most of the infected cells. However, only 7·7 per cent of these cells formed pocks on the chorioallantois.

Concurrent experiments on inhibition of clone formation by single cells taken from monolayers infected with the same virus seed, have shown that the proportion of cells which are prevented from dividing also corresponds to the input of HeLa plaque-forming units[4].

Since mitosis of the infected cells is inhibited, it follows that plaque formation is due to spread of infection to contiguous cells and this might obviously be due to release of virus. When single cells from infected monolayers were isolated in drop cultures, however, the number releasing infective virus was much less than the number of cells which gave rise to plaques. Thus in experiments with the same seed and dose as in the series quoted, where 43·6 per cent of cells formed plaques, none out of 30 cells released virus infective for HeLa cells, and only 3 in 80 (4 per cent) released virus detectable on the more sensitive chorioallantois.

If very few infected cells release virus capable of infecting HeLa cells or even chick cells, how then does the virus spread to the contiguous cells in a monolayer to cause the typical cytopathic effect? It is known that addition of antiserum after virus adsorption does not prevent the development of a plaque, which suggests that it does not depend on spread of released virus passing from cell to cell through medium. In addition, it has now been found that infected cells initiated plaques when they were added to monolayers in medium already containing strong antiserum. In two experiments 24 per cent and 10 per cent of cells formed infective centres in patients' antiserum (pock neutralization index 10^4) against 50 per cent and 36 per cent respectively in normal serum.

Multinucleate syncitia are a constant finding in HeLa cells infected with the *HFEM* strain of herpes virus, and it has been shown that these are due to cell fusion rather than nuclear division (ref. 5 and Stoker, M. G. P., and Newton, A., unpublished). The herpes plaque in its early stages consists, in fact, of a single syncitial mass with many nucleic and no intervening cell walls. These fused cells may be observed as early as 9 hr. after infection, and it is therefore possible that the virus spreads by fusion of an infected cell with its uninfected neighbours.

If virus does spread from cell to cell in this way by fusion of the cytoplasm it might be transferred as infective, but unreleased, virus particles, or alterna-

tively, in a vegetative, non-infective state. If it is due to infective virus, the latter ought to be detectable as such by disintegration of the cells at the end of the growth period.

Single cells from a monolayer infected as above were isolated in micro-drops and were burst by a single cycle of freezing and thawing after incubation for 30 hr., which was previously shown to be the optimal time for detecting released virus in single-cell cultures[2]. Only one cell in 130 (0·8 per cent) released HeLa-infective virus under these conditions, despite the fact that 43·6 per cent of the intact cells could give rise to plaques. In other experiments with a higher input (1·0 plaque-forming units per cell) and using the more sensitive pock assay, only 4 cells in 80 (5 per cent) released virus after freezing.

More thorough methods of cell disintegration and other sampling times will be needed to confirm the absence of infective virus in the majority of plaque-forming cells, but these results do raise the possibility that vegetative herpes virus can spread from cell to cell.

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Responses of Insects to Polarized Light in the Presence of Dark Reflecting Surfaces

The ways in which arthropods, such as bees[1–3], ants[4,5], Diptera[6], insect larvæ[7], Cladocera[8,9], Amphipoda[10] and Decapoda[11], orientate in respect to the plane of vibration of polarized light are controversial. Some authors have investigated by optical and electrophysiological means various arthropod eyes and their elements for the properties of an analyser[12,13], either those of a Nicol prism or those of some internal reflexion device; whereas others have been more concerned with external visual conditions[3] in which orientation to polarized light is observed, and have tried to explain it on the basis of mere brightness discrimination. The present communication has followed the latter approach and was based on the following considerations.

The three responses thus far used in demonstrating effects of light polarization, namely, the linearity of tracks, their angular orientation to the plane of polarization and responses to single sudden changes of this plane, are not phenomena which are very striking. It was thought that clearer results might be obtained in situations where continuous rotation of the plane of vibration would, by vectorial summation[14], induce strong rotatory optomotor reactions. Such a situation is provided in the apparatus shown in Fig. 1. This apparatus consists mainly of two coaxial circular turntables which can be moved independently of each other. On the upper one (drawn in black), which is mostly kept stationary, is placed an insect enclosed between two watch-glasses about 5 cm. in diameter. This turntable also carries a black cylinder and diaphragm shielding the insects from stray light. The lower and larger turntable carries a black cylinder covered either by a 'Polaroid' sheet or by a transparent sheet of plastic crossed in the middle by a black strip 3 cm. wide. This lower turntable can be turned by hand in either direction. The apparatus is placed in a dark room, 100 cm. beneath the open end of a piece of stove-pipe, 60 cm. long, which contains near its upper end a light bulb of about 100 W. Only about half the watchglass is visible to the observer when the apparatus is in position, and thus the direction of movement of an insect in it can be noted as it comes into view.

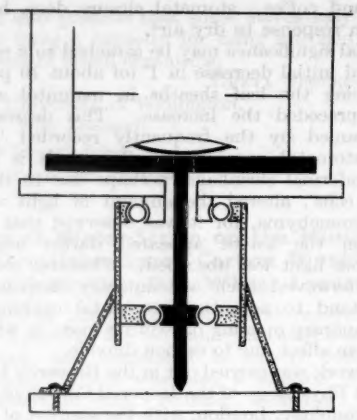

Fig. 1

Many species of flies, ants and moths were found to react to the rotation of light polarization. Table 1 summarizes the results of six typical experiments, each involving forty observations. It shows that (1) rotation of the plane of vibration induced clear optomotor reactions, but that (2) these occurred only in special visual circumstances, for example, when

Table 1. Reactions of Three Male *Aedes aegypti* (*a*, *b*, *c*), Two Female *Drosophila melanogaster* (*d*, *e*) and One Male *Thaumatomyia glabrosa* (*f*) to Forty Changes in the Direction of Rotation of a 'Polaroid' or a Strip

Bottom of watchglass	External cylinder carrying	Rotation of 'Polaroid' or strip changed to	Insect circling clockwise *a*	*b*	*c*	*d*	*e*	*f*	Insect circling following rotation* *a*	*b*	*c*	*d*	*e*	*f*
Covered with black passe-partout	'Polaroid' screen	clockwise 20 ×	16	14†	17	15	17	18						
		anticlockwise 20 ×	8	7†	3	3	2	3						
		total changes 40 ×	24	21	20	18	19	21	28	27	34	32	35	35
Transparent, standing on white paper	"Polaroid" screen	clockwise 20 ×	12	9	14†	8	13	13						
		anticlockwise 20 ×	11	10	13†	7	11	9						
		total changes 40 ×	23	19	27	15	24	22	21	19	21	21	21	24
Transparent, standing on white paper	Black strip, 3 cm. wide	clockwise 20 ×	12	12	17†	18	16	15						
		anticlockwise 20 ×	5	6	2†	1	5	6						
		total changes 40 ×	17	18	19	19	21	21	27	26	35	37	31	29

* Any number greater than 27 is significant at the 0·05 level. † Insect moving upside down.

the hollow of the lower watchglass was coated with black passe-partout (gum strip), whereas on a light background either no reaction or only a weak one occurred. Table 1 also shows that (3) optomotor responses similar to those induced by the 'Polaroid' were observed after a clear sheet carrying a black strip was substituted for it. The polarized light reflected from a white background towards the centre of the watchglass, where the insect's eyes were, is largely depolarized, and no great differences of intensity occur in different directions. On the other hand, a great deal of light is reflected from the black passe-partout in the plane of vibration, but very little vertically to it. Rotation of a 'Polaroid' thus results in the rotation of a light band in the dark part of the visual field of the insect. This effect can easily be demonstrated to the unaided human eye by means of a somewhat larger model. Findings (2) and (3) confirm the conclusions, derived from quite different experiments, of Baylor and Smith[3] on bees, namely, that some motor responses in insects are not induced by the polarized light directly perceived, but by light reflected from a dark background.

The above experiments do not, of course, preclude the possibility that the eyes of some arthropods, and perhaps of other animals, may have true analyser properties. Faint visual effects, comparable in intensity to the perception of Haidinger's figure by man[15], possibly occur widely; and stronger effects may occur in eyes possessing bulging lenses, like those of the Cladocera or of the tadpoles of *Xenopus*, where simple internal reflexion may operate[3]. Bees flying under large areas of polarized light from the sky[1] and insect larvæ crawling in the open[7] seem to react overtly to these large-scale patterns. On the other hand, in certain circumstances, when polarized light from a small source is reflected from dark reflecting surfaces, as in von Frisch's bees dancing on a horizontal comb[1,2], or in Santschi's ants crawling on sand inside a dark tube[4], maintenance of the perceived reflected light pattern provides a sufficient explanation. Attempts to explain reactions to light polarization by means of special, optical and nervous arrangements in the eye concerned and to demonstrate their existence by electrophysiological means, should in future be confined to visual situations, where the above explanation does not apply.

I wish to thank Prof. B. Hocking and Mr. W. Klaassen of the University of Alberta for help in these experiments, and Dr. E. R. Baylor of Woods Hole for sending me his mimeographed lecture notes.

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An Artificial Diet for the Laboratory Rearing of Locusts

Locusts are being increasingly used for research and teaching purposes, but one of the main difficulties involved in maintaining a culture is the provision of an adequate supply of fresh green grass throughout the year[1]. A further disadvantage of this grass diet was revealed by biochemical investigations into the variation with age of the concentration of reducing substances in the hæmolymph of *Schistocerca gregaria* Forsk., to be reported elsewhere. The above pattern of variation was partially masked by the considerable divergence of many results from the mean values. In view of these divergences, which were thought to be due to differences in the quality of the grass diet, an artificial diet was formulated. The use of this diet, to which very small quantities of fresh green grass were added, considerably reduced these divergencies.

Three series of experiments were later carried out in order to determine the effect of rearing both the desert locust *Schistocerca gregaria* Forsk. and the African migratory locust *Locusta migratoria migratorioides* (R. and F.) on (*a*) artificial diet alone, (*b*) artificial diet plus fresh green grass added once a week for 24 hr., and (*c*) artificial diet plus a very small quantity of fresh green grass given daily. In each series an equal number of control cages were set up in which the locusts were fed on fresh green grass given daily.

In all experiments the two species *L. migratoria* and *S. gregaria* were reared in initial batches of 20 in 12-litre cages of plastic and metal, kept in a constant-temperature room at 28° C., the temperature in the cages being 34–36° C. during the day and falling to 28° C. at night. This day temperature was maintained by placing five cages around each 100-watt bulb, which was on from 9 a.m. to 4 p.m. The relative humidities in both the control and artificial diet cages were 55–60 per cent in the mornings and 45–50 per cent in the late afternoons. Twigs, which were scarcely eaten during the course of the experiments, were placed in each cage to facilitate moulting by acting as perches. Each cage also

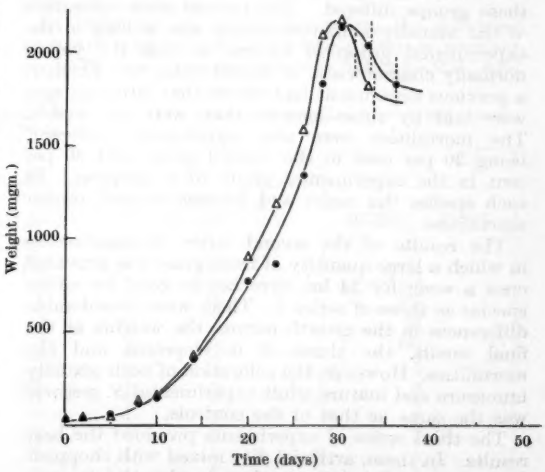

Fig. 1. Growth curves for *S. gregaria* females, series 1. —△—, Control (grass) diet; —●—, artificial diet. Final moult is indicated by broken vertical lines

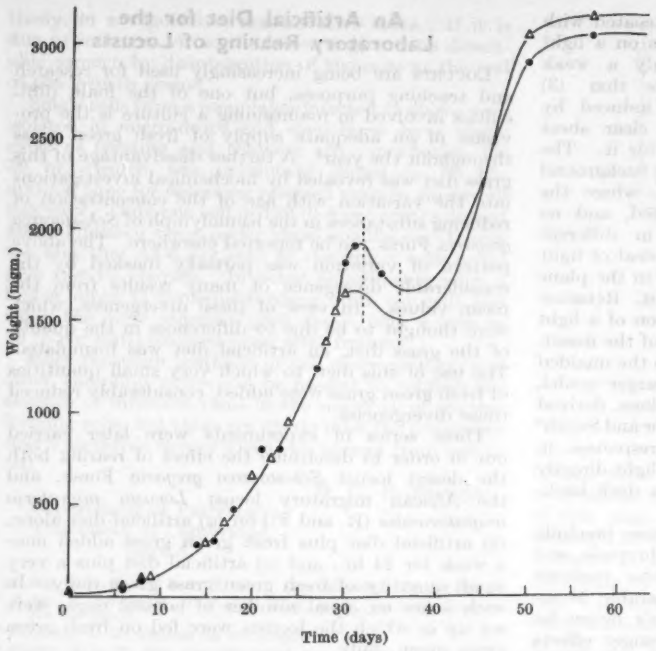

Fig. 2. Growth curves for *S. gregaria* females, series 3. —△—, Control (grass) diet; —●—, artificial diet. Final moult is indicated by broken vertical lines

had a dish containing cotton-wool soaked with water.

The artificial diet was offered as a dry mixture of the following composition: bran, 2; dried whole milk, 2; grassmeal, 2; dried brewers' yeast, 1 (parts by volume). The results of the first series of experiments in which artificial diet was fed to the experimental group of locusts are shown in Fig. 1.

Although the growth curves and weights at the final moult were similar for both the experimental and control groups of *S. gregaria*, the coloration of these groups differed. The normal pink coloration of the sexually immature adults was lacking in the experimental group of locusts, as was the yellow normally characteristic of sexual maturity. Further, a previous experiment had shown that although eggs were laid by these locusts, they were not viable. The mortalities were also significantly different, being 30 per cent in the control group and 80 per cent in the experimental group of *S. gregaria*. In each species the males and females showed similar mortalities.

The results of the second series of experiments in which a large quantity of fresh grass was provided once a week for 24 hr. were not so good for either species as those of series 1. There were considerable differences in the growth curves, the weights at the final moult, the times of development and the mortalities. However, the coloration of both sexually immature and mature adult experimental *S. gregaria* was the same as that of the controls.

The third series of experiments provided the best results. In these, artificial diet mixed with chopped-up grass was fed daily to the experimental locusts. The amount of grass supplied to each cage, in blades about $\frac{1}{4}$ in. wide, was equal to the sum of the lengths of locusts in that cage. Fig. 2 shows the growth curves for experimental and control females of *S. gregaria*.

In each species results for males and females were similar. With *S. gregaria* there was a tendency for the final moult of the experimental locusts to occur a few hours before and at a slightly greater weight than that of the controls. The mortalities were very nearly the same, averaging 28 per cent for the experimental locusts and 23 per cent for the controls. No difference in coloration could be detected up to the end of the sexually immature adult stage, although the normal yellow colour of the sexually mature males was acquired by the experimental locusts one week later than by the control group. Once the locusts were mature, the rate of laying of egg pods was the same, as was the period of incubation and the weight and colour of the emerging hoppers.

With *L. migratoria* the results for the three series of experiments were not so good, since the times of development were increased, the weights of all stages were reduced and the mortalities of experimental *L. migratoria* were considerably greater than those of the control group. These results are compatible with the fact that, in the field, the African migratory locust feeds mainly on grass whereas the desert locust does not.

It is therefore suggested that this artificial diet plus a small daily addition of fresh grass may be of use in maintaining cultures of *S. gregaria* in places where large quantities of fresh grass are not available throughout the year, the amount of grass required daily being of the order of 2–3 gm. for 50 adult locusts and correspondingly less for the preceding instars. The artificial diet alone may be useful in physiological and biochemical investigations on one instar where variations in diet tend to mask the changes due to development. In more extended studies the use of small quantities of a single species of grass grown throughout the year, in addition to the artificial diet, may also eliminate seasonal variations in diet. Full details of this work will appear elsewhere.

One of us (G. F. H.) wishes to thank the Agricultural Research Council for financial support in the initial stages of this work, and Prof. F. C. Happold and Dr. B. A. Kilby for their advice and encouragement, and for the hospitality of the Department of Biochemistry of the University of Leeds.

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Albinism in the Migratory Grasshopper, *Melanoplus bilituratus* (Wlk.)

HUNTER-JONES[1] discovered albinism in the desert locust, *Schistocerca gregaria* (Forsk.), and established an albino strain of this species. A single, nearly colourless, male of the migratory grasshopper, *Melanoplus bilituratus* (Wlk.)—formerly known as *M. mexicanus mexicanus* (Sauss.)—appeared in a culture at the Saskatoon laboratory in 1954. Although the characteristic as observed in this individual and his descendants may not conform to the strict definition of albinism, the term is retained here for its convenience.

The nearly colourless male was mated with a number of normal females of the same species, and the resulting F_1 progeny were all normally pigmented; the F_2 progeny contained a minority of grasshoppers resembling the albino parent, but the observed ratio of normal and albino individuals could not be reliably interpreted on a genetic basis. Later, male albinos were back-crossed to phenotypically normal F_1 hybrid females, and a progeny of about 500 was produced. This progeny was divided in the ratio of 238 albino : 257 normal ($\chi^2 = 0{\cdot}365$; $P = 0{\cdot}6$, basis 1 : 1 hypothesis). When both parents were albinos, only albino progeny were produced. The genetic basis of the albinism is therefore probably a single recessive gene.

In a mixed population of nymphs, albino individuals are not distinguishable by any means yet discerned until after the first nymphal moult; they are then unmistakable, though a slight expression of melanism persists. For example, the chevron pattern on the femora remains faintly discernible. In adults, a certain amount of rather diffuse melanic pigment appears and tends to intensify with age, although albino individuals remain easily distinguishable from normal ones throughout the adult life.

Albinos of *M. bilituratus* reared in the laboratory appear to grow as rapidly and to show the same degree of robustness and activity as normal individuals. In pure culture they appear to mate normally but a vigorously multiplying stock has not yet been produced; presumably egg production, or the viability of the eggs, is subnormal. Most of the albino individuals obtained have therefore been produced by matings involving at least one heterozygous parent. By successive breeding back to normal stock, it is hoped to overcome the apparent difficulties now encountered in maintaining a pure culture of albinos.

The survival value of the albino characteristic under natural conditions in western Canadian altitudes would be expected to be low, if only because individuals having the characteristic would presumably be unable to benefit from insolation to the same extent as the rather heavily melanized grasshoppers in the normal population.

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A New Type of Insecticide

RECENTLY, I found[1] that strains of *D. melanogaster* characterized by resistance to DDT, BHC, parathion and other insecticides were susceptible to phenylthiourea, while the majority of strains susceptible to DDT were resistant to phenylthiourea.

In previous papers[2,3] the genetical relation between resistance to phenylthiourea and to other insecticides has been discussed and the hypothesis was introduced that the dominant gene on the second chromosome, which confers resistance to DDT, BHC and parathion, also confers abnormal susceptibility to phenylthiourea. The dominant gene on the third chromosome which confers resistance to nicotine sulphate also confers resistance to phenylthiourea.

Accordingly, it may be presumed that susceptibility to phenylthiourea results from the pleiotropic expression of the dominant gene for resistance to DDT, BHC and parathion on the second chromosome. This assumption suggests that the mixture of DDT, BHC or parathion with a substance correlated negatively to these compounds, such as phenylthiourea, might have an effective insecticidal action and might not produce flies resistant to these mixtures even after continuous use.

In order to test this assumption, the following backcross was carried out by using a strain resistant to DDT and nicotine sulphate (Hikone-*R*31 wild

Table 1. THE NUMBER OF F_2-FLIES OF EACH PHENOTYPE IN THE BACKCROSS. (500 F_2 LARVÆ WERE USED FOR EACH TEST BY THE LARVAL TEST METHOD)

Phenotypes	*bw* ; *st ss*	*bw*	*st ss*	+
Genotypes	$\frac{bw}{bw}$; $\frac{st\ ss}{st\ ss}$	$\frac{bw}{bw}$; $\frac{st\ ss}{R\text{—}NS}$	$\frac{bw}{R\text{—DDT}}$; $\frac{st\ ss}{st\ ss}$	$\frac{bw}{R\text{—DDT}}$; $\frac{st\ ss}{R\text{—}NS}$
DDT, BHC, Parathion	*S*	*S*	*R*	*R*
Nicotine sulphate	*S*	*R*	*S*	*R*
Control	121	111	121	137
DDT 0·5 m*M*	18	9	110	116
DDT 1·0 m*M*	2	2	88	115
DDT 1·5 m*M*	0	0	90	98
DDT 2·0 m*M*	0	0	97	96
DDT 10·0 m*M*	0	0	99	101
PTU 3·0 m*M*	0	114	0	0
PTU 5·0 m*M*	0	109	0	0
PTU 3·0 m*M* DDT 0·5 m*M*	0	101	0	0
PTU 3·0 m*M* DDT 1·0 m*M*	0	71	0	0
PTU 3·0 m*M* DDT 1·5 m*M*	0	0	0	0
PTU 3·0 m*M* DDT 2·0 m*M*	0	0	0	0
PTU 5·0 m*M* DDT 0·5 m*M*	0	113	0	0
PTU 5·0 m*M* DDT 1·0 m*M*	0	75	0	0
PTU 5·0 m*M* DDT 1·5 m*M*	0	0	0	0
PTU 5·0 m*M* DDT 2·0 m*M*	0	0	0	0

The following abbreviations are used: *R*—DDT, DDT-resistant gene on the second chromosome; *R*—*NS*, nicotine sulphate-resistant gene on the third chromosome; *S*, susceptible; *R*, resistant; PTU, phenylthiourea.

strain) and a strain susceptible to DDT and nicotine sulphate (*bw* ; *st ss*, multichromosomal mutant strain) :

bw ; *st ss* ♀ × F_1 (*bw* ; *st ss* ♀ × Hikone-*R*31 ♂) ♂

The relation between the phenotypes and the number of surviving flies emerging from treated media was studied by using the larval test method[2]. Some of the results are shown in Table 1.

These results indicate that the mixed insecticide has a severe action even on flies exhibiting resistance to many kinds of insecticide. All strains of *D. melanogaster* were killed by exposing them to the mixture of the minimum amount of phenylthiourea which kills strains resistant to DDT and of the lowest amount of DDT which is enough to kill strains resistant to phenylthiourea (that is, susceptible to DDT).

Further experiments on the dosage from the point of view of population genetics are now in progress, and a more detailed report will be published elsewhere. I am greatly indebted to Prof. H. Kikkawa and Mr. M. Tsukamoto for supplying the strains resistant to insecticide.

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Fire-blight of Pear in England

The presence of fire-blight of pear, an extremely destructive bacterial disease caused by *Erwinia amylovora* (Burrill) Winslow *et al.*, has recently been confirmed in England. This represents the first authenticated record of the disease in Europe.

Fire-blight is indigenous to North America and has been known for more than 150 years in the United States, where it is still a major factor limiting the successful cultivation of pear in certain areas. Elsewhere it occurs only in New Zealand ; it appeared there about 1919 and in the next ten years spread to most fruit-growing areas of the Dominion. In addition to pear, the disease attacks apple and other related hosts, for example, quince, hawthorn, mountain ash, *Cotoneaster*, *Pyracantha* and various ornamental *Pyrus* spp.

The first intimation of the present outbreak was received during the late summer and autumn of 1957, from five fruit farms in the Maidstone, Wrotham and Rochester areas of Kent. Many pear trees of the variety Laxton Superb were then dying and on several others main branches had been killed by extensive cankers present on the branches and stems. In 1958 there was a further considerable spread of the disease in some of the affected orchards, and two completely new outbreaks were identified in the Rochester area.

Infection begins in the blossom, particularly the secondary blossom formed after the main spring flowering period. Diseased flower trusses turn black and the infection spreads rapidly into the branches causing a necrosis of the superficial cortical cells. The branches are eventually killed, the leaves wither and turn dark brown or black, and badly affected orchards then appear as if they have been swept by fire. The progress of the infection is halted towards the end of the season, but by this time it may have reached the trunk of the tree. Cracks now appear at the margins of diseased and healthy tissues and typical cankers are produced. In some of these cankers the bacteria survive the winter and renewed invasion of adjacent healthy tissues begins in the spring.

During the growing season, shoots and fruits may be attacked. These have an oily appearance at first but later they turn black in the same way as blossom. The fruits become wrinkled like a prune, and in humid weather they and the shoots exude a whitish bacterial ooze which turns amber after exposure.

The disease has been so destructive on Laxton Superb that one small orchard, consisting mostly of this variety, no longer has any commercial value. Conference, Dr. Jules Guyot and Bristol Cross have also been attacked, but so far only a few trees of these varieties have been involved. Williams Bon Chretien (*syn.* Bartlett), a variety often badly damaged by fire-blight in the United States, has so far remained virtually unaffected in the field, although it has shown little resistance in inoculation experiments.

Isolations made during this year from diseased branch, shoot, fruit and blossom tissues yielded the same organism, forming cream-coloured hemispherical colonies on a nutrient agar containing 5 per cent sucrose. The cross-infectivity of these isolates has been demonstrated in an extensive series of inoculation experiments. Symptoms on pear shoots and fruits were identical with those described for *E. amylovora*, the most characteristic feature being the production of white globules of bacterial ooze on the surface of infected tissues under humid conditions. Apple fruits, and apple and hawthorn shoots have also been successfully infected.

The pathogen is a Gram-negative peritrichous rod of the genus *Erwinia*, closely resembling authentic strains of *E. amylovora* in culture. The close affinity of the two organisms is also shown by tests with bacteriophages, isolated from soil in one of the diseased orchards by a method previously described[1]. Thus, among a wide range of *Erwina* and *coli-aerogenes* species examined, the phages were specific for the present pear isolates and *Erwinia amylovora*, including a strain of the latter tested at the New York State Agricultural Experiment Station, Geneva, U.S.A., by Dr. R. M. Gilmer.

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Autoradiographic Analysis on Agar Plates of Labelled Antigens from Rat Liver

In the study of protein metabolism it is often essential to be able to refer the incorporation of isotopic amino-acids to some individual type of protein, characterizable, for example, by means of a particular enzymatic activity or by its antigenic specificity[1]. As shown previously, soluble proteins derived from microscopic and submicroscopic fractions of liver cells can be characterized immunologically by means of precipitin reactions in agar plates[2]. In order to analyse some of the early pathways occurring in protein metabolism under various conditions, an attempt was then made to combine this method of protein identification with autoradiography in isotope incorporation experiments. A

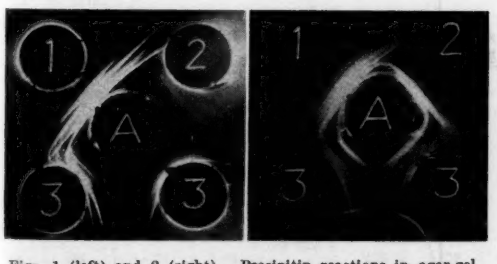
short account of the procedure and the results obtained are given in this communication[3].

Rat liver slices, about 0·3 mm. thick, were incubated for 30 min. in a Krebs–Henseleit medium in an atmosphere of 95 per cent oxygen and 5 per cent carbon dioxide. The medium, fortified with glucose, contained per ml. 0·015 μmole L-leucine-^{14}C (11·5 mc./mmole), 0·02 μmole of L-valine-^{14}C-(8·5 mc./mmole) and 0·065 μmole of DL-tyrosine-^{14}C (0·09 mc./mmole). The incubation was performed in tubes containing 40 mgm. of slices (fresh weight) per ml. of solution. After the incubation the slices were washed and homogenized in ice-cold 0·25 *M* sucrose. Microsomes and the soluble fraction were prepared by means of differential centrifugation[4]. The microsomal fraction was extracted with 0·4 per cent sodium deoxycholate[5]. Before further use, the solutions were diluted to contain approximately 4–6 mgm. protein/ml., determined according to Lowry *et al.*[6].

The immunological experiments were performed with antisera from rabbits, previously injected with total homogenate, microsomes or the soluble fraction ('supernatant') of rat liver. The mode of preparation of the antisera and the method of double diffusion in agar have been described previously[2].

After completion of the serological reactions the agar plates were freed from salts, amino-acids and excessive protein by prolonged washing with buffered saline and with water. After desiccation, the glass slides with the thin agar film on top were placed in contact with a photographic emulsion (Ilford, X-ray film, double coated) and left in the dark room for ten weeks. The autoradiographs were then developed in the usual way. Finally, the immunological precipitates were stained with azocarmin *B*[7], mounted with liquid plastics and the precipitation patterns recorded photographically.

Figs. 1 and 2 show the results of an experiment where the deoxycholate extract of microsomes was allowed to react with the various antisera mentioned above. Fig. 1 shows the normal spectrum of precipitates already described[2]. Fig. 2 presents the autoradiograph of the same experiment. Obviously, a high incorporation has been obtained of the amino-acids labelled with carbon-14 into the immunologically distinct proteins, extractable from the microsomes with deoxycholate. Moreover, the method has a good resolving power; the radioactivity is entirely concentrated to the different antigen–antibody precipitates, which show up almost as sharply in the autoradiograph as they do in the original plate.



Figs. 1 (left) and 2 (right). Precipitin reactions in agar-gel. Antigens diffusing from the central basin, antisera from the peripheral basins. Fig. 1 shows the print obtained by placing the dried agar film with the stained precipitates directly into the photographic enlarger. Fig. 2 shows the autoradiograph of the same plate. *A*, Deoxycholate extract of microsomes; 1, anti-microsomal serum; 2, anti-supernatant serum; 3, anti-total homogenate serum

As can be seen from Fig. 2, two strongly labelled precipitation lines were obtained in the reaction between the microsomal extract and the anti-supernatant serum. One of these also appeared between the extract and the anti-total homogenate serum. It is of great interest that the corresponding precipitates were scarcely visible in the original plate (cf. Fig. 1.) Although care must be taken in the interpretation of band-densities in the Ouchterlony reaction, there was good evidence to indicate that the amount of antigen in these heavily labelled precipitates was very low. Hence, it may be concluded that these two precipitates represent two groups of metabolically particularly active proteins.

The experiment described in this communication may be sufficient to illustrate the usefulness of a combination of autoradiography with immunological agar techniques for the qualitative and semi-quantitative analysis of protein metabolism in highly complex systems. Further studies on this method and its application are in progress.

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Coat-Colour and Longevity in Thoroughbred Mares

Authorities differ on the reality and consistency of differences in temperament and performance between horses of different colours[1,2]. Scheiermann[3], in a paper not available in Britain, has reported significant differences associated with colour in the working life of Rhenish horses. I have recently constructed life-tables for English thoroughbred mares, using the data contained in the General Stud Book, as part of a comparative study of the rates of actuarial ageing in mammals. Details of this work will appear elsewhere[4]: it was based on the 11 annual cohorts of brood mares foaled in 1860–64 and 1875–80 from the time of their entry at stud (average age 4 years). Of these 11 cohorts, 5 (1875–79) were scored for coat colour: of 1,271 mares composing them, 568 were bays, 181 browns, 262 chestnuts, 27 blacks, 5 greys, 3 roans and 2 grey roans, the balance being of doubtful or unstated colour. For comparison of the rarer coat-colours among thoroughbreds, further records of greys and blacks were taken by a search of the remainder of the Stud Book.

The mean and median expectations of life from 4 years of the various coat-colours, of the 1860–64 and 1875–80 samples, and of the individual cohorts making up the second of these, are given in Table 1. No separate life-table was calculated for brown mares, because of the probable diversity of coat-colours included in this description.

Table 1. Longevity and Survival by Coat-colour of Thoroughbred Mares

Group	n	$e_{x=4}$	V_0	Median
All colours :				
Foaled 1875	285	17·26	0·34	22·43
1876	245	17·65	0·21	22·43
1877	233	17·44	0·21	22·49
1878	248	17·49	0·30	22·15
1879	261	16·13	0·16	20·81
1880	221	16·01	0·18	21·81
1875–80	1,492	17·04	0·046	22·18
1860–64	1,250	17·31	0·044	22·07
Bays (1875–79)	568	16·68	0·08	22·03
Blacks (1854–1900)	358	16·53	0·15	21·95
Chestnuts (1875–79)	262	17·23	0·20	22·50
Greys (1845–1920)	200	15·57	0·28	20·43

Of the colour groups examined, only greys appear to diverge significantly from the mean expectations calculated for all mares, the difference being greater than those found between annual cohorts ($P < 0{\cdot}01$). Owing to the way in which the data were obtained, factors of selection cannot be entirely excluded ; the difference in the period from which lives of greys were drawn does not appear to be responsible for their shorter life, since there is no significant difference between the early and recent chronological halves of the sample. Greys have been selectively exported at most periods, compared with other coat-colours : they therefore show a rather higher percentage of losses to the record. Most of the reduction of their expectation of life is due to early deaths (< 10 years), the expectations of further life at 10 and 15 years being 10·96 and 3·85 years in greys as against 11·17 and 2·93 years in all mares of the 1875–80 sample. Causes of death were not recorded, and there is consequently no information about the prevalence of benign or malignant melanomata, to which grey horses of certain breeds are subject[5].

Grey thoroughbreds in the Stud Book are the progeny of a relatively small number of stallions compared with other colours, but none of these contributed sufficient progeny dying at a known age for the life-tables of his grey and non-grey fillies to be satisfactorily compared. Further studies of the Stud Book may indicate whether the apparent shortening of the life of grey thoroughbreds is real, and with what other factors it is correlated.

This work was undertaken during the tenure of a Nuffield Research Fellowship in Gerontology.

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Temperature Dependence of the Conductivity of Electrolyte Solutions

It has been known for some years that the ionization constant, K, of weak acids reaches a maximum value at a certain temperature T_m, which is defined by $T_m = \sqrt{(A_1/A_3)}$ if K is given by the following function of the absolute temperature[1] :

$$\ln K = -\frac{A_1}{T} + A_2 - A_3 T \qquad (1)$$

Here A_1 and A_3 are positive constants, while A_2 may be positive or negative. Equation (1) is valid for all kinds of solvents.

Kraus observed as early as 1900[2,3] that the conductance of non-aqueous salt solutions, when plotted against temperature, first increases, passes through a maximum and, thereafter, continues to decrease until the critical temperature of the solvent is reached. This phenomenon was ascribed by him to a continuous decrease of the dissociation constant for ion-pair formation with increasing temperature[4], which can only occur in solvents of a fairly high dielectric constant ε. (In these media the product εT, determining K, decreases as T increases.)

It is possible, however, to combine both phenomena and to give a more quantitative explanation of the conductance effect.

Combination of equation 1 with the fundamental electrochemical equations giving the relationship between ionic dimension (Stokes' law) and mobility, viscosity of the solvent and degree of ionization of the electrolyte, gives the following relation between the conductivity $\varkappa$ (in ohms^{-1} cm.$^{-1}$) of the solution and the absolute temperature :

$$\ln \varkappa \approx -\frac{\frac{A_1}{2} + \frac{\Delta E}{R}}{T} + A_4 - \frac{A_3}{2} T \qquad (2)$$

in which ΔE denotes the activation energy of viscous flow, R the gas constant per mole and A_4 is another constant, independent of temperature.

As $\Delta E/R$ is positive, it follows from equation 2 that $\ln \varkappa$ will reach a maximum value at the temperature :

$$T_m = \sqrt{\left\{\left(A_1 + \frac{2\Delta E}{R}\right)\Big/ A_3\right\}}$$

Thus it is clear that the effect observed by Kraus is a general phenomenon, valid for all electrolytes that are slightly ionized in the solutions considered.

By choosing a suitable solvent composition, the maximum in the conductivity can be brought into

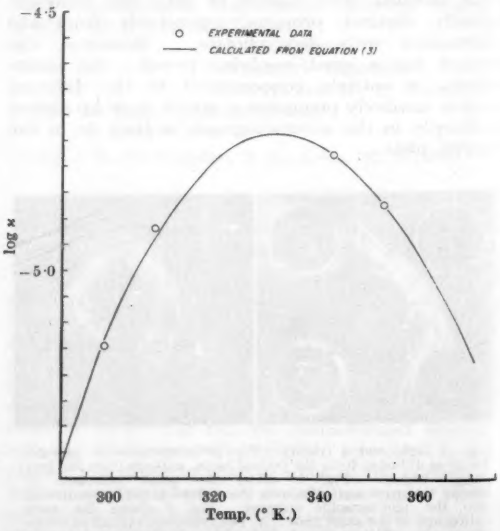

Fig. 1. Temperature dependence of the conductivity of 0·01 *N* acetic acid in water–dioxan (1 : 1 v/v)

a more accessible temperature region than Kraus observed. Examples are:

(1) 0·01 N acetic acid in water–dioxan (1 : 1 v/v), $T_m \approx 60°$ C.;

(2) 0·009 N perchloric acid in ethanol–benzene (21 : 34 v/v), $T_m \approx 60°$ C.

The first example is illustrated by Fig. 1. The conductivity curve drawn has been calculated from:

$$\log \varkappa = -\frac{11{,}760}{T} + 66{\cdot}14 - 0{\cdot}107\,T \qquad (3)$$

The coefficients in this equation have been determined from the experimental results.

Further details will be published elsewhere.

My thanks are due to Dr. E. A. M. F. Dahmen for his interest in this investigation.

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Change of Inclination of a Satellite Orbit

IN a recent article, Merson and King-Hele[1] state that the inclination of the orbit of satellite 1957β decreased by about 0·15° during its life and that this could not be accounted for by any effect of the Earth's ellipticity. The decrease appears to be a consequence of the cross-wind produced by the Earth's rotation.

If α is the inclination, λ the latitude, β the angular distance from apex, Ω the angular momentum, T the period and D the length of a sidereal day, then the track crosses the lines of latitude at an angle $\sin^{-1}(\sin\alpha \sin\beta \sec\lambda)$. The angle between the track and the apparent wind is $\tan^{-1}\left(\frac{T}{D}\sin\alpha \sin\beta\right)$ and this produces a couple about the line of apices the magnitude of which is a fraction $\frac{T}{D}\sin\alpha \sin^2\beta$ of that of the retarding couple. For a satellite rotating in the same direction as the Earth and impulsively retarded at perigee:

$$\frac{d\alpha}{dt} = \frac{T}{\Omega D}\sin\alpha \sin^2\beta \frac{d\Omega}{dt}$$

For an orbit of small eccentricity T is proportional to Ω^3 so that:

$$\frac{d\alpha}{dT} = \frac{\sin\alpha \sin^2\beta}{3D}$$

Table 1

T (min.)	Age (days)	β (degrees)	$\sin\alpha \sin^2\beta$	$\delta\alpha$ (degrees)	α (calc.)	α (obs. ± 0·02)
103·8	0	−31	0·24		65·321°	65·331°
				−0·015		
101	53·5	−51	0·55		306	309
				−0·027		
98	98	−71	0·81		279	272
				−0·034		
95	132·5	−86	0·90		245	232
				−0·036		
92	152·5	−96	0·90		209	204
				−0·030		
89·5	160	−99	0·89		179	192

It is seen that the values found for the variation of α can be fitted to Merson and King-Hele's curve within the observational error; the variation is therefore predictable and gives no information not otherwise attainable.

In view of this there seems no point in elaborating the analysis to take account of the spread of the resistance around perigee and the effects of the following wind and the variation with height of the angular velocity of the atmosphere.

C. H. BOSANQUET

"Dingestow",
Fairfield,
Stockton-on-Tees.
Sept. 30.

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Irregularities of Satellite Drag and Diurnal Variations in Density of the Air

A MARKED change in the slope of the period – time curves of *Sputnik* 2, *Sputnik* 3 and *Sputnik* 3 rocket has been reported, and from this it has been thought probable that the density of the air at a height of 220 km. increases considerably[1] somewhere between lat. 35° N. and 28° N.

An alternative explanation is that the sudden increase in drag is associated with the passage of the perigee from the night-side to the day-side of the Earth. In this case, the change is brought about chiefly by the precession of the orbital plane, instead of by the rotation of the perigee in the orbital plane. As the orbital plane rotates, the perigee is taken from the night-side to the day-side of the Earth, into air that has just been carried through the day-time side by the Earth's rotation; this being in the opposite sense to that of the orbital plane.

As the orbital plane precesses about ten times faster than the perigee rotates in the orbital plane, this explanation seems to account for the suddenness of the change more easily. An appreciable arc of the orbit near perigee could pass from the night-side to the day-side of the Earth in less than a day at the time of year when the terminator is at its smallest inclination (1·4°) to the orbital plane. At its greatest inclination (48°) to the orbital plane, the change-over would take about ten days.

For *Sputnik* 2, it is found that perigee passed into sunlight on December 23, 1957, the angle between orbit and terminator being nearly maximum. The observed change in slope of the period–time curve occurred over an interval of several days centred at about December 30. For *Sputnik* 3, rocket and satellite, the perigees passed into sunlight on July 13 and 14, 1958, the angle between orbit and terminator being nearly a minimum, whereas the observed changes in the slope of the period–time curves appear in the region of July 20 and 24 respectively. The correspondence is very close, and the consistent difference of about a week would be reduced if the calculated dates were based on a solar zenith distance of slightly less than 105°, which is the zenith distance of the horizon as seen from a height of 220 km. When the Sun's zenith distance increases beyond about 85°, the heat input would fall off rapidly due to the increasing length of path through the atmosphere. Assuming the cooling process to be of the same order of rapidity, so that 85° is the solar zenith distance at which the change occurs instead of 105°, the calculated dates

become December 29, 1957, for *Sputnik* 2 and July 20 and 22, 1958, for *Sputnik* 3, rocket and satellite.

Other dates on which the perigees of the Russian Earth satellites passed or will pass into daylight (solar zenith distance less than 85°) are March 19, 1958, for *Sputnik* 2, October 24, 1958, for *Sputnik* 3 rocket, and October 30, 1958, January 30, 1959, for *Sputnik* 3 satellite.

The dates on which the perigees passed or will pass out of daylight (solar zenith distance greater than 85°) are February 4, 1958, for *Sputnik* 2, June 11, September 6 and December 12, 1958, for *Sputnik* 3 rocket and June 9, September 9 and December 14, 1958, for *Sputnik* 3 satellite. The existence of a sharp *fall* in air density at perigee on these dates depends on the rate of heating of the night air as it passes into sunlight. This may be so slow that the change in the slope of the period – time curve is not detectable against the fluctuations due to changes in the aspect of the rocket.

Clearly, more observations are needed before variations in density in the upper atmosphere and the processes causing them can be fully understood. The solar heating which appears to be responsible for the increase of density at 220 km. probably occurs at much lower heights, perhaps in the region of 100 km., and the expansion of the air at this level lifts the atmosphere above. The use of spherical satellites would eliminate the fluctuations in the period – time curve due to changes of aspect of the rocket, and allow variations in density to be studied with very much greater precision. It should then be possible to follow tidal variations of air density. These have not so far been picked out and are largely unknown at great heights.

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London, W.C.1. Oct. 24.

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Secondary Oscillations in an Equatorial Atlantic Deep-Sea Core

Primary oscillations, corresponding to long-period changes in temperature in the upper layer of the sea, have been reported in long cores from Equatorial and North Atlantic, the Caribbean and Mediterranean Seas[1–3]. These changes, apparently the equivalent of glacial and interglacial periods, have been followed by: oxygen-18/oxygen-16 measurements on selected species of Foraminifera which deposit their tests in the upper layer of the sea; determining the proportions of planktonic Foraminifera characteristic of warm, temperate and cool waters; carbonate analyses and grain size determinations.

Cores from Atlantic abyssal plains are unsuitable for determining these changes because in these environments sediment is transported on the deep-sea floor from higher to lower levels. An undisturbed chronological sequence of sediments is frequently found in cores from the flat tops of isolated knolls, because they are outside the zone of turbidity currents.

Investigations have been made to determine whether undisturbed cores retain records of short-period temperature oscillations. A continuous series of ½-cm. sections have been taken from a core collected by the Swedish Deep-Sea Expedition (1947–48), from the top of a knoll in 1° 10′ N., 19° 50′ W. In this core the ratio of the sinistral to dextral tests of *Globigerinoides sacculifera* frequently changes by 20 per cent in ½ cm. It would therefore seem unlikely that the original sedimentary sequence has been appreciably disturbed by benthonic organisms.

Secondary carbonate oscillations, tentatively ascribed to short-period changes in temperature in the upper layer of the sea, were found superimposed on long-period changes[4]. It is unlikely that these oscillations are due to other causes because similar changes have now been found by determining in this core the annual rates of accumulation of: (1) calcium carbonate; (2) nitrogen; (3) fractions coarser than 500 and 250μ; (4) *Globorotalia menardii menardii*; and (5) *Globigerinoides sacculifera*. In collaboration with Dr. C. Emiliani and Mrs. T. Mayeda, oxygen-18 determinations have been made on the tests of *Globigerinoides sacculifera* isolated from 33 sections. There is a general parallelism between isotopic temperatures and rates of accumulation of calcium carbonate. It is, however, impossible to show by this technique whether the secondary carbonate oscillations are or are not reflexions of changes in temperature, because its accuracy is only about ± 1° C.

The age of the mid-point of each section, as well as its age range, was determined from the weights of titanium and iron in unit-area columns through each section. There is a variety of evidence which suggests that the rates of accumulation of these elements have not varied during the time interval represented by the core, and that there has been no post-depositional movement.

Some of the results, for the period 14,500 B.C.–4500 B.C., are shown in Fig. 1. There is at many points a sympathetic relation between the various methods. The rate of accumulation of *Globorotalia menardii menardii* was ~ 0·005 μgm./cm.²/yr. during the maximum phases of the last glaciation. The

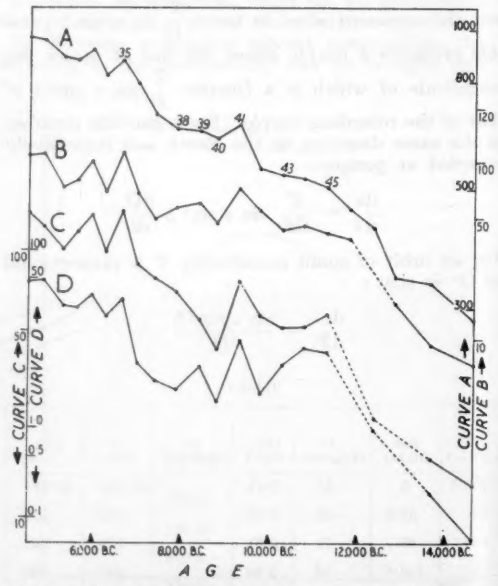

Fig. 1. Rates of accumulation (μgm./cm.²/yr. on a log scale) of: (*A*) calcium carbonate; (*B*) fraction coarser than 500μ; (*C*) *Globorotalia menardii menardii* plus *Globigerinoides sacculifera*, and (*D*) *Globorotalia menardii mendardii*. Section Nos. are given on curve *A*

maximum rate, ~ 159 μgm./cm.²/yr. was attained in about A.D. 1200. Confirmation is therefore given to Schott's hypothesis[5] that in the equatorial Atlantic this species was rare during the maximum phase of the last glaciation.

The reliability of all the methods of determining past changes in temperature is subject to various conditions—for example, methods (3), (4) and (5) are affected by changes in the degree of fragmentation. Methods (4) and (5) are invalidated if the investigated species replaces, or is replaced by, another species characteristic of warm water. The sharp rise in the rate of accumulation of *Globorotalia menardii menardii* between section Nos. 43 and 45 (Fig. 1*D*) is apparently related to this effect, because there is no notable increase in the combined rates of accumulation of *Globorotalia menardii menardii* and *Globigerinoides sacculifera* (Fig. 1*C*).

Thirty of the minor changes in the annual rates of accumulation of calcium carbonate may be correlated with secondary climatic changes in Europe and North America. For example, the oscillation at 9200 B.C. (section No. 41) is correlated with the well-established climatic amelioration in pollen zone II (the Alleröd oscillation). The radiocarbon age of zone II*b* at Wallensen, Germany, is 9200 B.C.[6], and its equivalent in eastern Wisconsin—the Two Creeks interval—has been dated by Arnold and Libby as 9450 B.C.[7]. The temporary return to cold in zone III is represented by section Nos. 40–39 (8750 B.C.–8350 B.C.). In Denmark the ages of the lower and upper limits of the Younger Dryas are, respectively, 8900 B.C. and 8350 B.C.[8], while its equivalent in eastern Wisconsin—the Valders glacial maximum—is dated 8700 B.C.[9].

The period of increasing temperature, 7850 B.C. (section No. 38)–6600 B.C. (section No. 35), apparently corresponds in Europe to the retreat of ice from the central Swedish moraines, and the Yoldia marine transgression in the Baltic. In the southern North Sea peat beds, containing a Maglemose harpoon-head[10], were apparently flooded after 6450 B.C.[11]. It is of interest to report that a small ridged flake of grey flint (British Museum, 1957, 663) was collected south of the Dogger Bank (53° 50·5′ N., 1° 40·0′ E.) in July 1957 by Lieut.-Commander C. J. de C. Scott while in command of H.M.S. *Shackleton*. Dr. K. P. Oakley considers that this could be Upper Palæolithic or Mesolithic.

In North America there is a period of increasing warmth marked by the rapid retreat of the ice from the Valders moraines in Wisconsin to those near Cochrane, Canada[12].

In view of the apparent correlation between secondary changes in the upper layer of the equatorial Atlantic and climatic changes in Europe and North America it is desirable, on climatological grounds, to discover whether similar oscillations occurred in other oceans. Cores from the Indian Ocean, collected by the John Murray Expedition (1933–34) and housed in the British Museum (Natural History), although unsuitable for detailed work of this nature, clearly indicate past temperature changes in the upper layer of this ocean. It is therefore hoped that when the preliminary programme for work in the Indian Ocean suggested by the Special Committee on Oceanic Research[13] is reviewed, consideration will be given to the desirability of collecting undisturbed cores from suitable sedimentary environments, and the necessity of training research students in the various techniques.

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Sept. 25.

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Polarographic Study of Acid-Base Reactions of the Tropylium Ion

A POLAROGRAPHIC study of the tropylium ion ($C_7H_7^+$) in unbuffered media[1] did not permit any quantitative interpretation of the acid-base phenomena at the surface of the mercury dropping electrode. We therefore followed the reduction of the tropylium ion in well-buffered media. At concentrations lower than about 0·00015 *M* one irreversible reduction wave was observed. The height of this wave decreased with increasing *p*H in the form of a dissociation curve (Fig. 2) with $pK' = 5{\cdot}64$ at $t_1 = 3{\cdot}3$ sec. The kinetic current at higher *p*H values is limited by the rate of formation of the reducible tropylium cation from electro-inactive

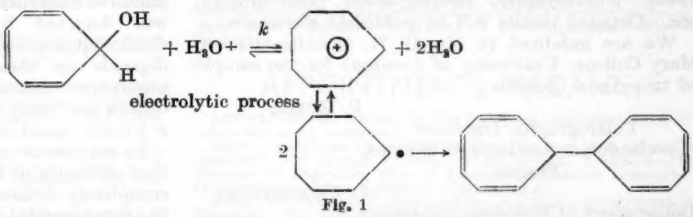

Fig. 1

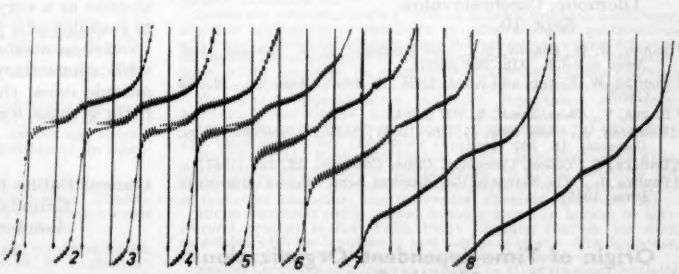

Fig. 2. Dependence on *p*H of the reduction of tropylium bromide. 0·0001 *M* tropylium bromide in Britton–Robinson buffers. (1) *p*H 2·4; (2) *p*H 2·8; (3) *p*H 3·1; (4) *p*H 4·0; (5) *p*H 4·8; (6) *p*H 5·2; (7) *p*H 5·9; (8) *p*H 6·6. $t_1 = 3{\cdot}3$ sec., $m = 2{\cdot}6$ mgm./sec. The complete deflexion corresponds to 0·1 μamp., 206 mV./abscissa. The small wave at more negative potentials is an oxidation product with carbonyl function

tropyl alcohol, which is present in the solution and is brought by diffusion to the surface of the mercury electrode.

The reduction proceeds by a one-electron step to a radical, with subsequent formation of ditropyl, as in the reduction by zinc[2]. The formation of the dimer was proved[3] by the shift of the half-wave potential with increasing tropylium bromide concentration. The half-wave potential at *p*H lower than 4·6 is independent on the *p*H; at higher *p*H it shifts to more negative values according to the equation $E_{1/2} = -0{\cdot}25 - 0{\cdot}040\ p\mathrm{H}$ (standard calomel electrode). The slope of the curves is 0·040. All the phenomena observed are consistent with the mechanism indicated in Fig. 1.

Neither the character of the dissociation curves nor the pK' values are affected by the buffer components, by the pyridinium ions or by the ionic strength. Using the equation derived by Koutecký[4] and the value $pK = 4{\cdot}6$, determined by titration, the rate constant for the formation of tropylium ion was calculated as $k = 2 \times 10^6$ l. mole^{-1} sec.$^{-1}$.

At concentrations of the tropylium ion higher than about 0·001 *M*, three types of adsorption processes were observed. Using the value for the lowest adsorption wave, the surface-area (*S*), covered by one reduced seven-membered ring at the surface of the mercury drop, was calculated by Brdička's equation[5] as 29 A.^{2}. Using covalent radii and bond distances[6], *S* was calculated as 22 A.^{2}. Adsorption processes were studied using *i*–*t* curves, *i*–*t* curves, single-sweep polarography, oscillographic polarography, etc. Detailed results will be published elsewhere.

We are indebted to Mr. C. R. Ganellin (Queen Mary College, University of London) for the sample of tropylium bromide.

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Sept. 10.

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Origin of Time-dependent Organization in a Micelle Series

The question of physical equilibrium in homogeneous solution may be stated as follows: At what stage of molecular complexity can a solute exist in non-equilibrium for times which are very long in relation to the scale of molecular processes? The complex linear micelles formed by the interaction of naphthol and a quaternary soap are able to exist[1] and, contrary to expectation[2], the simple micelles formed by the same soap alone[3]. The purpose of this communication is to show at what point in a homologous series such persistent non-equilibrium arises.

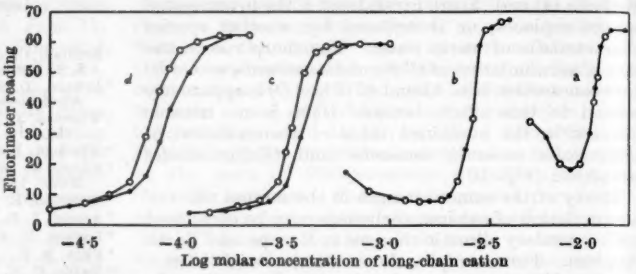

Fig. 1. Use of fluorescent dye in discriminating between different states of a cationic soap solution. Fluorescence of μM dichlorofluorescein as a function of concentration of four cationic soaps at 25° C. *a*, C12 trimethyl ammonium bromide in 4 m*M* sulphate; *b*, C14 in 0·24 m*M* sulphate; *c*, C16 in 0·05 m*M* sulphate and *d*, C18 in 0·024 m*M* sulphate. ○, Stock soap added to diluted salt; ●, stock salt added to diluted soap

The compounds chosen were the C12, 14, 16 and 18 paraffin-chain trimethyl ammonium bromides, in aqueous solution around the critical micelle concentration, with a low concentration of sodium sulphate to develop the non-commutative property. This meant that the chemical potential could depend on the order in which the components were added (from relatively strong stock solution) as well as on the final composition. Sulphate was used rather than halide to minimize supersaturation[4]. Non-equilibrium was detected by fluorescence quenching, using dichlorofluorescein as the marker. The method depends on the sensitiveness of the dye/micelle adsorption complex to chemical potential; full details are being submitted elsewhere together with a theory based on accepted principles.

In numerous experiments at 25° C. it was found that solutions of the C12 and C14 soaps were always completely defined by their composition, so that all the experimental points fell on a single curve (Fig. 1). This was not true for the others; the curve split into two parts, the upper part referring to solutions in which sulphate had been added first, and the lower to those in which soap had been added first, as predicted by theory. The possibility of superimposable organization in homogeneous solution seems, therefore, to arise at a very early stage in molecular complexity, in micelles of a paraffin-chain salt with 16 or possibly 15 carbon atoms. Because of water-structure effects with quaternary compounds[4,5], not apparent with anionic ones, the critical chain-length is probably a little greater for the latter.

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FORTHCOMING EVENTS

*(Meetings marked with an asterisk * are open to the public)*

Monday, December 1

ROYAL SOCIETY (at Burlington House, Piccadilly, London, W.1) at 2.30 p.m.—Anniversary Meeting.

BRITISH SOCIETY FOR THE HISTORY OF SCIENCE, PHILOSOPHY OF SCIENCE GROUP (in the Joint Staff Common Room, University College, Gower Street, London, W.C.1), at 5.30 p.m.—Dr. R. S. Peters: "A Defence of Aristotelianism in Psychology".

SOCIETY OF ENGINEERS (at the Geological Society, Burlington House, Piccadilly, London, W.1), at 5.30 p.m.—Mr. T. J. Hawker: "Some Industrial Applications of Magnetic Power".

UNIVERSITY OF LONDON (in the Physiology Lecture Theatre, University College, Gower Street, London, W.C.1), at 5.30 p.m.—Prof. Z. M. Bacq (University of Liège): "Substances which Protect Against Ionizing Radiations"*. (Further lecture on December 3.)

ROYAL INSTITUTE OF CHEMISTRY, LONDON SECTION (joint meeting with the LONDON SECTION of the SOCIETY OF CHEMICAL INDUSTRY, at the Society of Chemical Industry, 14 Belgrave Square, London, S.W.1), at 6.30 p.m.—Dr. J. L. Edgar: "The Production of Petrochemicals in Holland".

ROYAL GEOGRAPHICAL SOCIETY (at 1 Kensington Gore, London, S.W.7), at 8.30 p.m.—Mr. A. R. Akester: "Saharan Survey".

Tuesday, December 2

UNIVERSITY COLLEGE (in the Physiology Theatre, Gower Street, London, W.C.1), at 5.30 p.m.—Dr. W. S. Feldberg: "Some Physiological Aspects of General Anæsthesia".*

INSTITUTION OF MECHANICAL ENGINEERS, EDUCATION GROUP (at 1 Birdcage Walk, Westminster, London, S.W.1), at 6 p.m.—Discussion on "The Planning of Mechanical Engineering Teaching Laboratories".

SOCIETY OF CHEMICAL INDUSTRY, CORROSION GROUP (at 14 Belgrave Square, London, S.W.1), at 6.30 p.m.—Discussion of Three Research Papers published in the *Journal of Applied Chemistry*.

Wednesday, December 3

UNIVERSITY OF LONDON (at the Postgraduate Medical School of London, Ducane Road, London, W.12), at 2 p.m.—Dr. R. I. S. Bayliss: "Laboratory Investigations in Endocrinology".*

SOCIETY FOR ANALYTICAL CHEMISTRY (joint meeting with the ASSOCIATION OF PUBLIC ANALYSTS, at the Wellcome Building, Euston Road, London, N.W.1), at 3 p.m.—Symposium on "Food Analysis"

ROYAL STATISTICAL SOCIETY (at the London School of Hygiene and Tropical Medicine, Keppel Street, Gower Street, London, W.C.1), at 5.15 p.m.—Discussion on the Report of the Committee on the Supply of and Demand for Statisticians.

INSTITUTE OF FUEL (at the Institution of Civil Engineers, Great George Street, London, S.W.1), at 5.30 p.m.—Mr. G. W. Lee: "The Work of the British Coke Research Association".*

INSTITUTE OF PETROLEUM (at 61 New Cavendish Street, London, W.1), at 5.30 p.m.—Mr. J. F. Hutton: "Flow Properties of Distillates at Low Temperatures: a Review"; Mr. H. Strawson: "The Pumpability of Aviation Turbine Fuels at Low Temperatures".

UNIVERSITY OF LONDON (in the Anatomy Theatre, University College, Gower Street, London, W.C.1), at 5.30 p.m.—Prof. O. E. Lowenstein, F.R.S.: "Sensory Function and Qualitative Information".* (Further lectures on December 4 and 5.)

SOCIETY OF CHEMICAL INDUSTRY, PLASTICS AND POLYMER GROUP (at 14 Belgrave Square, London, S.W.1), at 6.30 p.m.—Mr. D. A. Boyle, Mr. W. Simpson and Dr. J. D. Waldron: "The Characterization of Short Chain Branches in Hydrocarbon Polymers".

RADAR AND ELECTRONICS ASSOCIATION (at the Royal Society of Arts, John Adam Street, Adelphi, London, W.C.2), at 7 p.m.—Dr. R. L. F. Boyd: "Exploration of the Upper Atmosphere by Rockets and Satellites".*

Thursday, December 4

ROYAL SOCIETY (at Burlington House, Piccadilly, London, W.1), at 10.30 a.m.—Discussion on "The Effect of Environment Upon Molecular Energy Levels" opened by Dr. H. W. Thompson, F.R.S.

LINNEAN SOCIETY OF LONDON (at Burlington House, Piccadilly, London, W.1), at 5 p.m.—Exhibition Meeting.

INSTITUTE OF REFRIGERATION (at the Institute of Marine Engineers, The Memorial Building, 76 Mark Lane, London, E.C.3), at 5.30 p.m.—Mr. G. L. H. Bird, Dr. J. C. Fidler, Mr. W. B. Gosney and Colonel H. Randal Steward: Review of the Moscow Meetings of the International Institute of Refrigeration.

INSTITUTION OF ELECTRICAL ENGINEERS (in conjunction with the BRITISH NUCLEAR ENERGY CONFERENCE, at Savoy Place, London, W.C.2), at 5.30 p.m.—Mr. D. W. Fry: "A Review of Work towards Nuclear Energy from Controlled Thermonuclear Reaction".

PHYSICAL SOCIETY, ACOUSTICS GROUP (in the Physics Department, Imperial College, London, S.W.7), at 5.30 p.m.—Dr. P. T. Haskell: "Insect Acoustics".

ROYAL ANTHROPOLOGICAL INSTITUTE OF GREAT BRITAIN AND IRELAND (at 21 Bedford Square, London, W.C.1), at 5.30 p.m.—Prof. C. von Fürer-Haimendorf: "Monastery and Village among the Sherpas of Nepal".

ROYAL INSTITUTION, LIBRARY CIRCLE (at 21 Albemarle Street, London, W.1), at 5.30 p.m.—Dr. A. S. C. Lawrence: "Sir James Dewar and the Royal Institution".

SOCIETY OF CHEMICAL INDUSTRY, MICROBIOLOGY GROUP (at 14 Belgrave Square, London, S.W.1), at 6.15 p.m.—Meeting on "Preparation of Vaccines". Dr. P. W. Muggleton and Miss J. P. Farmer: "Preparation and Standardization of Freeze-Dried B.C.G. Vaccine". Dr. J. A. Dudgeon: "Preparation of Viral Vaccines".

POLAROGRAPHIC SOCIETY (at "The Duke of York", 8 Dering Street, London, W.1), at 7 p.m.—Informal Discussion Meeting on "Some Polarographic Problems Encountered in the Food Industry" introduced by Dr. T. L. Parkinson.

ROYAL INSTITUTE OF CHEMISTRY, LONDON SECTION (joint meeting with the Battersea College of Technology Chemical Society, at the Battersea College of Technology, Battersea Park Road, London, S.W.11), at 7 p.m.—Prof. A. R. Ubbelohde, F.R.S.: "Melting Mechanisms of Ionic Crystals".

Thursday, December 4—Friday, December 5

BRITISH INSTITUTE OF RADIOLOGY, incorporated with the ROENTGEN SOCIETY (at Church House, Westminster, London, S.W.1)—Annual Congress and Exhibition.

Friday, December 5

INSTITUTION OF BRITISH AGRICULTURAL ENGINEERS (at 6 Buckingham Gate, London, S.W.1), at 2.15 p.m.—Paper: "How Far are British Tillage and Harvesting Machines Meeting Overseas Conditions?" (Informal Meeting).

UNIVERSITY OF LONDON (at Senate House, London, W.C.1), at 5.30 p.m.—Dr. W. H. Glanville: "Motorways".*

SOCIETY OF CHEMICAL INDUSTRY, PESTICIDES GROUP (together with the AGRICULTURE GROUP and the FINE CHEMICALS GROUP, at 14 Belgrave Square, London, S.W.1), at 5.45 p.m.—Joint Meeting on "Gibberellic Acid". Dr. P. W. Brian: "The Effects of Gibberellic Acid on Plant Growth"; Dr. B. E. Cross: "The Chemistry of Gibberellic Acid".

INSTITUTION OF MECHANICAL ENGINEERS (in conjunction with the BRITISH NUCLEAR ENERGY CONFERENCE, at 1 Birdcage Walk, Westminster, London, S.W.1), at 6 p.m.—Mr. K. G. Mantle, Mr. N. Marshall and Dr. P. J. Palmer: "An Experimental Investigation into the Stress Distribution in a Band Reinforced Pressure Vessel".

SOCIETY OF DYERS AND COLOURISTS, LONDON SECTION (at the Royal Society, Burlington House, Piccadilly, London, W.1), at 6 p.m.—Dr. J. L. Stoves: "Dyeing of Furs".

ROYAL INSTITUTION (at 21 Albemarle Street, London, W.1), at 9 p.m.—Dr. Richard van der Riet Woolley, F.R.S.: "Stellar Motions and the Structure of the Universe".

Saturday, December 6

ASSOCIATION OF AGRICULTURE AND THE BRITISH AGRICULTURAL HISTORY SOCIETY (at the Institute of Education, University of London, Malet Street, London, W.C.1), at 11 a.m.—Agricultural History Conference.

APPOINTMENTS VACANT

APPLICATIONS are invited for the following appointments on or before the dates mentioned:

SENIOR LECTURER IN RADIOCHEMISTRY in the Department of Chemistry and Biology, College of Technology, Liverpool—The Director of Education, City of Liverpool Education Committee, 14 Sir Thomas Street, Liverpool 1 (December 5).

ASSISTANT LIBRARIAN (with a good honours degree) IN THE SCIENCE LIBRARIES—The Registrar, The University, Liverpool (December 6).

ASSISTANT PHYSICIST (with a good honours degree in physics) IN THE PHYSICS DEPARTMENT of the Sheffield National Centre for Radiotherapy—The Secretary, Sheffield Regional Hospital Board, "Broom Cross", Tree Root Walk, Sheffield 10 (December 6).

LECTURER (with a good honours degree in mining engineering and postgraduate research and/or industrial experience) IN MINING ENGINEERING—The Registrar, King's College, University of Durham, Newcastle-upon-Tyne (December 6).

CHAIR OF METALLURGY—The Registrar, The University, Manchester (December 8).

SCIENTIFIC OFFICER, Grade 3 (with an honours degree in metallurgy, chemical engineering or chemistry, or other academic qualifications and research achievements considered the equivalent), AT THE WEAPONS RESEARCH ESTABLISHMENT of the Department of Supply, near Adelaide, South Australia, for research into high-temperature materials with special reference to rocket motors and high-velocity rocket missiles—The Senior Representative (AV/9/12), Department of Supply, Australia House, Strand, London, W.C.2 (December 8).

LECTURER OR ASSISTANT IN ORGANIC CHEMISTRY—The Registrar, The University, Leeds (December 15).

POST-DOCTORAL RESEARCH FELLOW IN THE DEPARTMENT OF FUEL TECHNOLOGY AND CHEMICAL ENGINEERING, to direct and carry out research on the laws of smoke formation and elimination with all types of fuel—The Registrar, The University, Sheffield (December 15).

MICRO-BIOLOGIST (with a good honours degree in botany or agricultural botany) at the Welsh Plant Breeding Station, for work associated with the breeding of new strains of clover—The Registrar, University College of Wales, Aberystwyth (December 20).

SENIOR LECTURER or LECTURER (Grade I or II) IN GEOLOGY initially in the Geography Department, University College, Ibadan, Nigeria, to develop teaching of geology in the Faculty of Science and to assist with geology teaching for the Faculty of Agriculture—The Secretary, Inter-University Council for Higher Education Overseas, 29 Woburn Square, London, W.C.1 (December 22).

LECTURER IN THE DEPARTMENT OF ZOOLOGY, and an ASSISTANT IN THE DEPARTMENT OF ZOOLOGY—The Secretary, The University, Edinburgh (December 27).

FELLOW (with previous research experience in either radio astronomy or astronomy) IN RADIO ASTRONOMY in the Division of Radio Physics, Commonwealth Scientific and Industrial Research Organization, Sydney, to take part in an active research programme in some aspect of radio astronomy—Chief Scientific Liaison Officer, Australian Scientific Liaison Office, Africa House, Kingsway, London, W.C.2, quoting Appointment No. 780/194 (December 31).

SENIOR LECTURER or LECTURER IN AGRICULTURAL BOTANY, a LECTURER IN INORGANIC CHEMISTRY, a LECTURER IN MATHEMATICS, and LECTURERS (2) IN BOTANY at the University of Khartoum—The Secretary, Inter-University Council for Higher Education Overseas, 29 Woburn Square, London, W.C.1 (December 31).

LECTURER (electrical engineer or physicist) IN ELECTRICAL ENGINEERING—The Registrar, University College of South Wales and Monmouthshire, Cathays Park, Cardiff (January 13).

CHAIR OF AGRICULTURAL CHEMISTRY—The Registrar, University College of Wales, Aberystwyth (January 17).

SENIOR FELLOW or FELLOW (with qualifications, interests and experience in some physico-chemical aspect or aspects of biochemistry) IN THE DEPARTMENT OF PHYSICAL BIOCHEMISTRY, John Curtin School of Medical Research, Australian National University, Canberra—The Secretary, Association of Universities of the British Commonwealth, 36 Gordon Square, London, W.C.1 (Australia, January 19).

ASSISTANT, Grade B (graduate, preferably with teaching and/or industrial experience) IN PHYSICS, to teach up to B.Sc. and H.N.C. standard—The Clerk to the Governors, Mid-Essex Technical College and School of Art, Market Road, Chelmsford.

ASSISTANT LECTURER, Grade B (with a degree or equivalent qualification, and preferably industrial and/or research experience) IN CHEMISTRY—The Principal, Medway College of Technology, Horsted, Maidstone Road, Chatham, Kent.

ASSISTANT LECTURER, Grade B (with an honours degree in geography and teaching experience), IN GEOGRAPHY, preferably with Social Studies as subsidiary subjects—The Principal, Coventry Technical College, Coventry.

BIOCHEMIST IN THE ENDOCRINOLOGY LABORATORY—The House Governor, Royal Marsden Hospital, Fulham Road, London, S.W.3.

BRADFORD CITY COUNCIL RESEARCH SCHOLAR (honours graduate in chemistry or biochemistry) IN THE DEPARTMENT OF CHEMICAL TECHNOLOGY, to work on some aspect of protein chemistry related to the keratins—The Registrar, Institute of Technology, Bradford 7.

EXPERIMENTALIST (physical or inorganic chemist, preferably with a degree) IN THE ELECTROMAGNETIC SEPARATION TEAM investigating the chemistry of most elements including plutonium, using many physical and engineering techniques—The Group Recruitment Officer (1249/34), U.K.A.E.A., Atomic Energy Research Establishment, Harwell, Berks.

LECTURER or SENIOR LECTURER IN METALLURGY in the Department of Mechanical Engineering—The Registrar, Royal Technical College, Salford 5.

LECTURERS and SENIOR LECTURERS (with an honours degree in engineering or equivalent qualification) IN THE DEPARTMENT OF MECHANICAL ENGINEERING—The Registrar, Royal Technical College, Salford 5.

LIBRARIAN (woman, with a degree in biology or zoology)—The Secretary, Bureau of Animal Population, The University, Botanic Garden, Oxford.

RESEARCH PHYSICIST (preferably with experience in the use of ultra-high vacuum systems or in the chemical physics of surfaces) IN THE DEPARTMENT OF PHYSICS, for work involving electrical measurements applied to the study of surface contamination processes on semiconductors—The Professor of Physics, University of Reading, Physics Research Laboratories, Upper Redland Road, Reading, Berks.

SCIENTIFIC OFFICER (CHEMIST) (with a good honours degree in chemistry, postgraduate experience in food analysis, and preferably a knowledge of fumigant and insecticide analysis) IN THE DEPARTMENT OF MARKETING AND EXPORTS, Federation of Nigeria, to undertake research into problems associated with the storage of oil seeds and other food crops with particular reference to insect infestation with the object of evolving methods for reducing losses—The Director of Recruitment, Colonial Office, London, S.W.1, quoting BCD.153/14/05.

SCIENTIFIC OFFICER (with a good honours degree in botany or agriculture, and preferably some postgraduate experience in agronomic methods and a knowledge of field experimentation statistics) WITH THE WEST AFRICAN MAIZE RESEARCH UNIT, Nigeria, to take charge of agronomic work with maize and to conduct trials in maize husbandry—The Director of Recruitment, Colonial Office, London, S.W.1, quoting BCD.197/375/02.

SENIOR AGRONOMIST (with a university degree in agriculture or a degree in natural science with a postgraduate diploma in agriculture and experience in field experimental studies, preferably with perennial tree crops) AT THE WEST AFRICAN COCOA RESEARCH INSTITUTE, Ghana, to take charge of the Agronomy Section and co-operate with senior specialist officers in the field of experimental work of the Institute—The Director of Recruitment, Colonial Office, London, S.W.1, quoting BCD.197/200/010.

SENIOR HISTOLOGICAL TECHNICIAN—Prof. H. P. Gilding, Department of Physiology, Medical School, Birmingham 15.

REPORTS and other PUBLICATIONS

(not included in the monthly Books Supplement)

Great Britain and Ireland

Engineering Materials and Design, Vol. 1, No. 1 (October, 1958). Pp. 58+48A. Published monthly. Annual subscription 35s.; 5.25 dollars. Single copies 2s. 6d. (London: Heywood and Co., Ltd., 1958.) [239

Hill Farming Research Organisation. First Report, 1954–58. Pp. 88. (Edinburgh: Hill Farming Research Organisation, 1958.) [239

Government of Northern Ireland: Ministry of Agriculture. Leaflet No. 123: Fowl Paralysis and Related Conditions in Poultry. Pp. 5. (Belfast: Ministry of Agriculture, 1958.) [239

Northern Advisory Council for Further Education. Eleventh Annual Report for year ended 31st March, 1958. Pp. 26. (Newcastle upon Tyne: Northern Advisory Council for Further Education, 1958.) [239

University Grants Committee. University Development 1952–1957. Pp. 92+8 plates. (Cmnd. 534.) (London: H.M. Stationery Office, 1958.) 5s. 6d. net. [239

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The Development of High Tensile Aluminium Bronze Alloys for Marine Propellers in Great Britain and the United States of America. Pp. 26. (London: The Mond Nickel Company, Ltd., 1958.) [239

National Museum of Wales. Illustrated Guide. Pp. 39+12 plates. (Cardiff: National Museum of Wales, 1958.) 1s. 6d. [239

Report of Her Majesty's Civil Service Commissioners for the period 1st April, 1957 to 31st March, 1958. (92nd Report.) Pp. 32. (London: H.M. Stationery Office, 1958.) 2s. net. [239

A Survey of Science. By Dr. Max Pattersson. Pp. iii+37. (London: Science Club, 1958.) 7s. 6d. [239

Microscopic Staining Techniques, No. 2. By Edward Gurr. Second edition. Pp. 62. (London: Edward Gurr, Ltd., 1958.) 6s.; 1 dollar. [299

University of Bristol: Department of Economics (Agricultural Economics). Report No. 106 (April, 1958): Grassland in England and Wales (with special reference to the Bristol II. Province). By V. H. Beynon. Pp. 59. (Newton Abbot: University of Bristol, Department of Economics, 1958.) 5s. [299

Institute of Navigation. Report of the Council, 1957–58. Pp. 14. (London: Institute of Navigation, 1958.) [299

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Bericht über das Geobotanische Forschungsinstitut Rübel in Zurich für das Jahr 1957. Von E Rübel und W. Lüdi. Pp. 114. (Zürich: Geobotanische Forschungsinstitut Rübel, 1958.) [239

East Africa High Commission. East African Agriculture and Forestry Research Organization. Record of Research for the period 1st July, 1956 to 31st December, 1957. Pp. vii+112. (Nairobi: Government Printer, 1958.) Sh. 3/50. [239

Colony of Mauritius. Annual Report of the Observatory Department, 1956. Pp. ii+12. Meteorological Observations and Climatological Summaries. January, 1957. Pp. ii+13. February, 1957. Pp. 13. March, 1957. Pp. 13. April, 1957. Pp. 13. May, 1957. Pp. 13. June, 1957. Pp. 13. (Port Louis: Government Printer, 1958.) [239

Annals of the New York Academy of Sciences. Vol. 72, Article 6: The Influence of Sulfhydryl Groups and Their Inhibitors on the Distribution of Radiocobalt in the Organs and Intracellular Organelles of the Mouse. By Laurence S. Maynard. Pp. 227–238. Vol. 73, Article 1: Hodgkin's Disease. By Antonio Rottino and 33 other authors. Pp. 1–380. Vol. 73, Article 2: Surgical Convalescence. By F. Curtis Dohan and 19 other authors. Pp. 381–538. Vol. 76, Article 1: Periodic Table for Fundamental Particles. By John J. Grebe. Pp. 1–16. (New York: New York Academy of Sciences, 1958.) [299

Metropolitan Life Insurance Company. Statistical Bulletin, Vol. 39 (August, 1958): Poliomyelitis Today. Our Rising Educational Level. Accidents Among School-Age Children. The Increasing Dominance of Chronic Disease. Pp. 12. (New York: Metropolitan Life Insurance Company, 1958.) [299

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Ministerio de Agricultura de Colombia: Oficina de Investigaciones Especiales. Boletin Miscelanea, No. 1: Investigacion Agricola en "Tibaitata." Pp. xi+70. Boletin de Divulgacion, No. 4: Diacol Nutibara: Una Nueva Variedad de Frijol. Por C. Cardona, O. Barros and R. L. Skiles. Pp. 15. (Bogota: Ministerio de Agricultura de Colombia, 1957 and 1958.) [299

Inter-American Tropical Tuna Commission. Annual Report for the year 1957. Pp. 134. (La Jolla, Calif.: Inter-American Tropical Tuna Commission, 1958.) [299

Wissenschaftliche Ergebnisse der Deutschen Atlantischen Expedition aus dem Forschungs- und Vermessungsschiff *Meteor*, 1925–1926. Herausgegeben im Auftrage der Deutschen Forschungsgemeinschaft von A. Defant. Band 5: Temperatur, Salzgehalt und Dichte an der Oberfläche des Atlantischen Ozeans. Dritte Lieferung: Untersuchungen über die Mittleren Hydrographischen Verhaltnisse an der Meeresoberfläche des Nördlichen Nordatlantischen Ozeans. Von Wolfgang Krauss. Pp. 251–410. (Berlin: Walter de Gruyter & Co., 1958.) 57 D.M. [299

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